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For: HYDROGEL COMPOSITES AND SUPERPOROUS HYDROGEL COMPOSITES HAVING FAST SWELLING, HIGH MECHANICAL STRENGTH, AND SUPERABSORBENT PROPERTIES	:	Confirmation No: 1689

DECLARATION UNDER 37 CFR 1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

We, Kinam Park, Jun Chen and Haesun Park hereby declare the following:

1. We are the co-inventors of claims 1-40 in the above-identified patent application.
2. We did conceive and reduce to practice the claimed invention prior to May 7, 1997.
3. In support of the fact that the claimed invention was completed prior to May 7, 1997, we refer to the attached Exhibit A, entitled "Synthesis of Superporous Hydrogel Composites with Fast Swelling, High Mechanical Strength,

and Superabsorbent Properties." Exhibit A is a photocopy of our original invention disclosure document (sans Figures). That document was prepared by us and sent by Federal Express courier to the law firm, Lowe, Price, LeBlanc & Becker, on December 16, 1996 for preparation and filing of the above-identified patent application.

4. The document contained in Exhibit A proves conclusively that the claimed invention was conceived and reduced to practice prior to May 7, 1997.

We further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

12/6/06	Kinam Park
Date	Kinam Park
12/6/06	Jun Chen
Date	Jun Chen
12/6/06	Haesun Park
Date	Haesun Park

Attachment: Exhibit A (39 pages)

EXHIBIT A

SYNTHESIS OF SUPERPOROUS HYDROGEL COMPOSITES WITH FAST SWELLING, HIGH MECHANICAL STRENGTH, AND SUPERABSORBENT PROPERTIES

Kinam Park, Jun Chen, and Haesun Park

I. SUMMARY OF THE INVENTION

This invention relates to a technique for the preparation of superporous hydrogels and superporous hydrogel composites which swell fast to a very large size and yet maintain high mechanical strength. More specifically, this invention relates to a technique of synthesizing various types of superporous hydrogels and superporous hydrogel composites, drying with minimum alteration of the porous structures of superporous hydrogels and superporous hydrogel composites, and their potential applications in various fields. Superporous hydrogel composites are superporous hydrogels synthesized in the presence of composite materials such as microparticles of crosslinked sodium carboxymethylcellulose, crosslinked sodium starch glycolate, or crosslinked polyvinylpyrrolidone (PVP). The composite materials are chemically crosslinked to polymer chains of superporous hydrogels. The presence of such composite material or materials increases the swelling speed substantially without altering the superabsorbent property of the dried superporous hydrogels, and dramatically enhances the mechanical property of the fully swollen superporous hydrogels. The process of making superporous hydrogel composites can also be applied to the making of conventional hydrogel composites, which also dramatically enhance the mechanical strength of the hydrogels without significantly altering the swelling kinetics and the extent of swelling.

The superporous hydrogels and superporous hydrogel composites are ideal in the preparation of platforms for oral controlled drug delivery systems, diet control device, superabsorbent for personal hygiene products, fast absorbing material for blood during surgery, and separation vehicles for biotechnology products such as bioactive peptides and proteins. The superporous hydrogel composites can also be made biodegradable using biodegradable crosslinking agents.

II. BACKGROUND OF THE INVENTION

A hydrogel is a crosslinked polymer network which is insoluble in water but swells to an equilibrium size in the presence of excess water. The research on hydrogels started in 1960s with a landmark paper on poly(hydroxyethyl methacrylate) by Wichterle and Lim (1). Due to the unique properties of hydrogels and potential applications in various areas including controlled drug delivery, various types of hydrogels have been synthesized and characterized since then. Much of the work on hydrogels has been concentrated on lightly cross-linked, homogeneous homopolymers and copolymers. One of the limiting factors in the application of hydrogels has been the rather slow swelling property of dried hydrogels, which are essentially glass. For the dried hydrogels to swell, water has to be absorbed into the glassy matrix of the dried hydrogels. The swelling kinetics of the dried hydrogels thus depends on the absorption of water occurring by a diffusional process and the relaxation of the polymer chains in the rubbery region. Equilibrium swelling of dried hydrogels in an ordinary tablet size (e.g., 1 cm in diameter x 0.5 cm height) usually takes at least several hours, and this may be too slow for many applications where fast swelling is essential. For example, hydrogels

diameter x 0.5 cm height) usually takes at least several hours, and this may be too slow for many applications where fast swelling is essential. For example, hydrogels have been successfully used as a gastric retention device that can stay in the stomach of a dog for up to 60 hours (2,3). In those studies, however, hydrogels had to be preswollen for a few hours before administering to the dog to avoid premature emptying into the intestine.

To overcome the slow swelling property of dried hydrogels, we have synthesized superporous hydrogel which can swell within minutes regardless of the size of the matrix (4). While the superporous hydrogels provided significantly fast swelling kinetics and high swelling extent, the mechanical strength of the fully swollen superporous hydrogels was too poor to be useful. In some cases, the fully swollen superporous hydrogels could not be picked up and easily broken due to the very poor mechanical properties. Usually, mechanically strong superporous hydrogels can be made by increasing the crosslinking density, but this would result in very small extent of swelling with a loss of superabsorbent property. Thus, making superporous hydrogels with fast swelling and high absorbency as well as with high mechanical strength was necessary. This disclosure deals with a technique to make such superporous hydrogels, more specifically superporous hydrogel composites.

To understand the unique properties of superporous hydrogels, we will compare the various types of hydrogels and superporous hydrogels.

A. Hydrogels, Microporous Hydrogels, and Macroporous Hydrogels.

Hydrogels and superporous hydrogels can be made by either crosslinking water-soluble polymer chains or polymerizing hydrophilic monomers in the presence of crosslinking agents. Since polymerization of the monomers has been used extensively in the preparation of hydrogels and superporous hydrogels, we will use it here to describe various properties of the hydrogels and superporous hydrogels.

Polymerization of monomers in the absence of any other solvent is called bulk polymerization. Bulk polymerization of monomers, such as hydroxyethyl methacrylate (or HEMA), leads to a production of a glassy, transparent polymer matrix which is very hard. When immersed in water, such a glassy matrix swells to become soft and flexible. Although it allows the transfer of water and some low molecular weight solutes, this kind of swollen polymer matrix (i.e., hydrogel) is considered non-porous. The pores between polymer chains are in fact the only spaces available for the mass transfer, and the pore size is within the range of molecular dimensions (a few manometers or less) (5). Under a scanning electron microscope, the surface of the dried hydrogels appears completely nonferrous. In this case, the transfer of water or other solutes is achieved by a pure diffusional mechanism (5). This restricts the rate of absorption and to some extent the size of species that are absorbed (6). The homogeneous hydrogels have been used widely in various applications, especially in the controlled drug delivery area where limited diffusional characteristics are required (7).

Hydrogels are usually prepared by mixing monomers with suitable solvent, and such a polymerization is known as solution polymerization. The nature of a synthesized hydrogel, whether a compact gel or a loose polymer network, depends on the type of monomers, the amount of diluent in the monomer mixture (i.e., monomer-diluent ratio), and the amount of crosslinking agent (8). As the amount of diluent (usually water) in the monomer mixture increases, the pore size also increases up to the micrometer (μm) range (5). Hydrogels with the effective pore sizes in the 10~100

"macroporous" are used interchangeably simply due to the fact that there is no unified definitions on micro- and macro-pores in hydrogels. Hydrogels with pores up to 10 μm can be described as either microporous or macroporous hydrogels.

It is important to distinguish definitions on microporous and macroporous structures in hydrogels and those in non-hydrogel porous materials, such as porous polyurethane foams. In the plastic foam area, micro- and macro-pores were indicated as pores less than 50 μm and pores in the 100~300 μm range, respectively (9). One of the reasons for this difference is that the hydrogels with pores larger than 10 μm were rarely made, while porous plastics with pores in the 100~300 μm range are very common. Porous hydrogels with pore size larger than 100 μm were made only recently (10,11), and that is probably why the definitions on porous hydrogels are different from those in porous plastics.

Microporous and macroporous hydrogels are sometimes called polymer sponges (5). When a monomer, hydroxyethyl methacrylate (HEMA), is polymerized at the initial monomer concentration of 45 (w/w)% or higher in water, a hydrogel of poly(HEMA) (or PHEMA) is produced with a porosity higher than homogeneous PHEMA hydrogels. These heterogeneous PHEMA hydrogels are sometimes called "sponges" in the biomedical literature (5,12). This term "sponge" is not recommended, since it is better known as the "rubber sponge" which is not a hydrogel in any sense. Furthermore, the properties of rubber sponges are totally different from porous hydrogels. For example, rubber sponges release imbibed water upon squeezing, but porous hydrogels are not squeezable. Porous hydrogels break into pieces with water entrapped into the polymer networks because of their hydrophilic nature.

B. Superporous Hydrogels

Superporous hydrogels are a new type of hydrogels which have numerous supersize pores inside them. Panels A and B in Fig. 1 are the scanning electron microscopic (SEM) pictures of dried superporous hydrogels at two different magnifications. Panel C in Fig. 1 is the SEM picture of dried, conventional hydrogels. As clearly seen in the three pictures, superporous hydrogels have numerous pores while the conventional hydrogels show no pores throughout the matrix even under SEM. The size of pores in superporous hydrogels is larger than 100 μm, usually in the range of several hundreds micrometers, and can be up to the millimeter range. Most of the pores inside of the superporous hydrogel are connected to form the open channel system. The size and number of the pores can be controlled by adjusting the type and amount of surfactant and gas forming agent during crosslinking polymerization. Even after drying, the pores of the superporous hydrogels remain all connected each other to form capillary channels. Panels D and E are drawings of superporous hydrogels (D) and conventional hydrogels (E) based on a scanning electron microscopic pictures. These two drawings highlight the differences between the superporous hydrogels and conventional hydrogels. Because of this, dried superporous hydrogels can swell extremely fast upon contact with water and swell to a very large size.

It should be noted that the superporous hydrogels have distinctly different properties compared to the microporous and macroporous hydrogels. First, the size of pores in the superporous hydrogels is about several hundred micrometers and can increase up to the millimeter range, which is much larger than the pores in the microporous or macroporous hydrogels. Second, in contrast to conventional microporous or macroporous hydrogels which contain relatively small fraction of

empty spaces, the superporous hydrogels can easily accommodate gas cells more than several hundreds percent of the volume of the starting monomer mixtures. Third, pores in the superporous hydrogels remain connected even after drying, and this makes the dried hydrogels swell extremely fast.

C. Methods of Preparing Porous Hydrogels

1. Poro(si)gen technique

Porous hydrogels can be made by preparing hydrogels (usually polymerizing monomers) in the presence of dispersed water-soluble porosigens, which can be removed later by washing with water to leave an interconnected meshwork (i.e., porous hydrogels) (7,13). Examples of effective porosigens are micronized sucrose (7), lactose (7), dextrin (7), sodium chloride (12), and PEG (14).

Water itself can be used as a porosigen if a polymer network is formed in the frozen state. Monomers can be polymerized in the frozen state around aqueous crystals, and then water can be subsequently removed by thawing to result in a macroporous hydrogel (7,15). In this approach, which is appropriately called "freeze-thaw technique", ice crystals function as a porosigen.

When a polymer network is formed in an aqueous solution, the whole system can be freeze dried to sublimate ice crystals and leave a porous matrix (16). This "freeze-drying" technique is useful in the preparation of porous hydrogels from polymers such as polysaccharides (e.g., sodium alginate (17)). To prepare porous hydrogels more effectively using the freeze-drying technique, salt can be added as another porosigen, and this increases the reproducibility of preparing porous materials (9).

Non-aqueous solution can also be used as a porosigen in polymerization of the oil-in-water emulsion system (18). In this case, the water phase contains water-soluble monomers and a crosslinker and the oil phase is a volatile organic solvent. The continuous water phase is polymerized and this is followed by evaporation of the oil phase, which results in the porous structure.

The pore size of hydrogels prepared by the porosigen technique depends on the size of porosigens. The introduction of a porosigen reduces mechanical strength significantly, although such a negative change in mechanical properties can be minimized if the size of the porosigen is maintained below 40 μm (7). In many cases where larger pores are necessary, microparticulate particles (e.g., sucrose crystals) in the range of 100~300 μm have been used (9). The presence of such large sized pores will obviously make porous hydrogels extremely weak.

2. Phase separation technique

In solution polymerization, monomers are usually mixed in a diluent which is good for both monomers and polymers. If, however, the diluent is a non-solvent for the polymer formed (e.g., PHEMA in water), the solubility of polymers dramatically decreases as the polymerization proceeds. This results in phase separation of the polymer-rich monomer phase into droplets, which then join together to form a network filled with large spaces (i.e., heterogeneous, porous hydrogels) by the end of polymerization process. This process is called heterogeneous solution polymerization (5,8,19).

Phase separation can also be induced from the initially homogeneous polymer solution by altering the solvent quality. The solvent quality can be decreased by removing good solvent or adding non-solvent to a polymer solution or by changing the temperature. Many polymer solutions form a reversible gel upon changes in temperature. For example, gelatin in water becomes a gel when cooled below the critical miscibility temperature (20). In general, aqueous polymer solution can be rapidly frozen to result in the spinodal decomposition, and subsequent removal of water by freeze-dry sublimation yields porous hydrogels. For polymers with the lower critical solution temperature (LCST), water becomes a non-solvent to the polymer and phase separation occurs as the temperature is increased above LCST. This technique has been used to prepare porous hydrogels made of poly(N-isopropylpolyacrylamide) (21-23), and crosslinked hydroxypropylcellulose (24). The pore sizes of macroporous hydrogels prepared by phase separation are typically only a few micrometers. In addition, the overall porosity is very low and this implies that the pores are not well interconnected. The major limitation of the phase separation method is that only very limited types of porous hydrogels can be prepared. In addition, there is not much control over the porosity of the gels when prepared by phase separation.

3. Crosslinking of individual hydrogel particles

Individual hydrogel particles can be crosslinked to form a crosslinked aggregates of particles. Pores can be formed between hydrogel particles. Such aggregate macrostuctures were prepared by initially mixing the hydrogel particles (in the range of a few hundred micrometers) with a solution of a crosslinking agent, water, and hydrophilic organic solvent such as isopropanol (25). Pores in such structures are present between hydrogel particles and the size of pores is much smaller than the size of particles. This approach is limited to the absorbent particles which has chemically active functional groups on the surface.

4. Gas blowing (or foaming) technique

Hydrogels can be prepared in the presence of gas bubbles. Monomers can be polymerized or water-soluble polymer chains can be crosslinked around gas bubbles generated by a blowing agent. The gas blowing technology has been widely used in the preparation of plastic foams using materials such as polyurethanes, rubber, and poly(vinyl chloride). The key ingredient in the foaming process is a blowing agent (or foaming agent) which is defined as any substance or combination of substances capable of producing cellular structure within a polymer matrix. Foaming agents are classified as physical foaming agent which expands when pressure is released (e.g., nitrogen and carbon dioxide) and chemical foaming agent which decompose or react to form a gas (e.g., sodium bicarbonate).

Recently, the gas blowing technique was used to prepare superporous hydrogels (10,11). Because of the technique used in the preparation of superporous hydrogels, they were also called "hydrogel foams." In the synthesis of superporous hydrogels by the gas blowing technique, foaming and polymerization have to occur simultaneously. For this reason, it is important to control the timing for foaming and polymerization. In the study mentioned above, inorganic carbonates, such as Na_2CO_3 and $NaHCO_3$, were used as a foaming agent. Those inorganic carbonates have long been used safely as a gas forming ingredient in effervescent tablets for antacids. They are safe, cheap, and easy to use.

We have successfully used the gas blowing technique to make superporous hydrogels of polyacrylamide, poly(sodium acrylate), poly(2-hydroxyethyl methacrylate), poly(hydroxypropyl methacrylate), poly(3-sulfopropyl acrylate, potassium salt), poly(2-acrylamido-2-methyl-1-propanesulfonic acid), poly({2-(acryloyloxy)ethyl}trimethylammonium methyl sulfate), poly(N-isopropyl acrylamide), poly(N-vinyl pyrrolidinone) (PVP), modified sucrose, and gelatin. Of course, many more different superporous hydrogels can be made by this method. The pore size of porous hydrogels prepared by the foaming technique is usually larger than 100 μm, and it can easily reach the millimeter range. Many times, the pores are so large that they can be visible by an unaided eye.

III. SYNTHESIS OF SUPERPOROUS HYDROGELS AND SUPERPOROUS HYDROGEL COMPOSITES

A. General Requirement for Preparation of Superporous Hydrogels with and without Composiste Materials

Superporous hydrogels were prepared by crosslinking polymerization of monomers in the presence of gas bubbles. Thus, synthesis of superporous hydrogels requires blowing agents and surfactants, in addition to the usual components for making hydrogels such as monomer, cross linker, and chemical initiator. Blowing agents generate gas bubbles and surfactants stabilize the generated foams by lowering the film-air interfacial tension and increasing the film viscosity (26).

There are two processes involved in the preparation of superporous hydrogels: polymerization and foaming. In order to make homogeneous superporous hydrogels, these two processes should occur about the same time. Thus, control of timing of the two processes is critical. To permanently capture the gas bubbles in the polymer network, the gelling must occur when the foam is stabilized. Since the foaming process is relatively short and it is difficult to stabilize a foam longer than a few minutes, the gelling has to start within a few minutes after the beginning of foaming (e.g., the addition of $NaHCO_3$ to the monomer mixture).

The fast gelling can be achieved by careful choice of monomers (type and concentration), initiators (type and concentration), temperature, and solvent. Typically, water soluble acrylates, methacrylates, and acrylamides gel very fast. In this study, most of the superporous hydrogels were made from these monomers. In addition, high monomer concentration, proper type of initiator, high initiator concentration, high temperature, and good solvent can all increase the polymerization rate.

Gas bubbles can be formed by any gas blowing method, either chemical or mechanical. In our study, $NaHCO_3$ was chosen as a blowing agent because of its unique advantages (as described below) that may not be provided by other techniques, such as thermal decomposition of chemical agent, mechanical whipping, volatilization of low-boiling liquid, chemical reaction, expansion of dissolved gas upon pressure release, incorporation of microsphere into a polymer mass, and expansion of gas-filled beads by heating (27). The amount of blowing agent, $NaHCO_3$ in our study, controls the pore size and the porosity of superporous hydrogels.

For large-scale production of superporous hydrogels, mechanical blowing through an atomizer might be a better choice than the chemical blowing method for

the following reason. In a large-scale production it may not be desirable to complete a polymerization in a few minutes because the heat generated during polymerization may not be dissipated quickly and cause a problem. Thus, smaller amount of initiator may be used to delay the gelling time (e.g., more than 10 minutes). Since mechanical blowing can start at any time for any duration, the foaming process may begin at the desired time and foam height can be maintained as necessary. Accurate timing control is possible by mechanical blowing in the large-scale production of superporous hydrogels.

B. Superporous Hydrogels Prepared in Aqueous Solution

1. Monomers, crosslinker, and initiators

Superporous hydrogels were synthesized from various monomers, such as acrylic acid (AA), acrylamide (AM), hydroxypropyl methacrylate (HPMA, Eastman Kodak Chemical Co.), N-isopropyl acrylamide (NIPAM), vinylpyrrolidone (VP), hydroxyethyl methacrylate (HEMA), 3-sulfopropyl acrylate (potassium salt, SPAK), 2-acrylamido-2-methyl-1-propanesulfonic acid (AMPS), and {2-(acryloyloxy)ethyl}-trimethylammonium methyl sulfate (ATMS). All monomers, unless specified, were obtained from Aldrich Chemical Company, Inc. The molecular structures of monomers used in this study are shown in Table 1. To ensure fast gelling, the concentration of monomers in aqueous solution was above 10% in most cases.

The redox pair of ammonium persulfate (APS) (Aldrich Chemical Co.) and N,N,N',N'-tetramethylethylenediamine (TEMED) (Bio-Rad Laboratories) were used as initiators, while N,N'-methylenebisacrylamide (Bis) (Aldrich Chemical Co.) was used as a cross-linker. In most of the superporous hydrogel preparation, the cross-linker concentration equivalent to 1% (w/w) of monomer was used. Too high cross-linker concentrations caused the swollen superporous hydrogels to become more fragile and to result in reduced swelling ratio. On the other hand, too low cross-linker concentrations caused the superporous hydrogels to become more soft and also fragile. The initiator concentration can significantly affect the polymerization rate. In this study, the concentrations of APS and TEMED were about 2% (w/w) of monomer. The gelling usually started within a few minutes after the addition of $NaHCO_3$.

2. Blowing agents and a trigger system

$NaHCO_3$ (Mallinckrodt Specialty Chemical Co.) was used as a blowing agent in the presence of an acid (acrylic acid, HCl, citric acid, or acetic acid) for the preparation of superporous hydrogels because the $NaHCO_3$-acid system exhibited advantages over other gas blowing techniques. It is safe, cheap, and easy to use. More importantly, it allows us to control the timing of bubble formation during the polymerization step. Acrylic acid or HCl was used in most cases. First, monomer, cross linker, acid, surfactant, and initiators were mixed. Then, $NaHCO_3$ was added to generate the gas bubbles. The foam size was determined by the amount of released gas bubbles which, in turn, was determined by the amount of acid and $NaHCO_3$. We used excess amount of $NaHCO_3$ and controlled the foam size by controlling the amount of acid. The reason is described below.

Two processes are involved in the superporous hydrogel preparation: polymerization and foaming as shown in Fig. 2. The solid line A-B-C represents the polymerization process. The dotted line D-E-F represents the foaming process. When APS/TEMED are used as initiators, the polymerization rate is pH-dependent. The

optimal pH for the initiators is 7~8. Under this pH range, the polymerization proceeds rapidly after the addition of initiator, and the gelling can start usually after 1~2 minutes. If the foaming starts too late, the solution can become too viscous for a good mixing, and it results in a non-homogeneous porous hydrogel. To make homogeneous superporous hydrogel, the time for the addition of the foaming agent must be carefully controlled over a very narrow viscosity range. Usually, this timing control is difficult. However, when acid and $NaHCO_3$ are used as the foaming agents, they provide a special trigger system that makes the timing control very easy.

In the beginning of polymerization (point A), all the ingredients for polymerization, except $NaHCO_3$, were mixed. The presence of acid reduced the pH to an acidic level (pH 5~6). Therefore, the TEMED-catalyzed free radical generation was inhibited because TEMED was protonated under this pH. This resulted in a very slow polymerization (A->B). At point D, $NaHCO_3$ was added. It reacted with acid and started the foaming process (D->E). In the meantime, the pH of the solution rose to a pH above the neutral level (i.e., pH 7~8). At this pH, TEMED (in the free base form) could catalyze the free radical generation from ammonium persulfate and started the accelerated polymerization (28). Consequently, the gelation proceeded rapidly (B->C) and completed at point C. Here, $NaHCO_3$ acted as a trigger for polymerization so that the foaming and polymerization could proceed in parallel. Therefore, no special timing control was needed. From E to F (E->F), the foam stayed at its maximum size in the presence of foam stabilizers. After point F, the foam would subside (if gelling did not occur). To make a good superporous hydrogel, the gelling should start when the foam is maintained in its maximum size. In other words, point C should be in between points E and F. In our study, the gelling occurred 1~2 minutes after the addition of $NaHCO_3$ so that the foam remained stabilized until the gelling started. We used excess amount of $NaHCO_3$ to ensure that the final pH was above neutral, and to control the foam volume by the amount of acid.

In general, the polymerization process is slow and the duration of maximum foaming (E->F) is short. Almost all of the monomers used in the synthesis of superporous hydrogels were acrylates and their derivatives, because they have relatively fast polymerization rate. The APS/TEMED system used in this study initiated the gelling of these monomers within a few minutes. To prolong the maximum foaming during gelling process, various foam stabilizers were used.

3. Foam stabilizers

A good foam stabilizer should be able to stabilize the foam until the beginning of the gelling process. We examined more than 30 different kinds of surfactants, such as Triton® surfactants, Tween and Span surfactants, Pluronic® surfactants (poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) tri-block copolymers) (BASF), Silwet® surfactants (OSi Specialties Inc.), sodium dodecyl sulfate (Bio-Rad Laboratories), albumin (Sigma Chemical Company), and gelatin. Pluronic® F127 (PF127) showed the best foam stabilizing property for most of the hydrophilic monomers used in the superporous hydrogel preparation. PF127 sustained the foam for the longest period of time. For relatively hydrophobic monomers, such as NIPAM or HPMA, PF127 alone did not provide good foam stabilizing effect. However, the proper combination of PF127, Pluronic® P105 (PP105), and Silwet® 7605 (SL7605) provided satisfactory foam stabilizing effect. SL7605 is a polyalkyleneoxide-modified polydimethylsiloxane surfactant. It was observed that too little surfactant could not provide enough foam stabilizing effect, but excess surfactant above a certain level

provide enough foam stabilizing effect, but excess surfactant above a certain level did not result in better foam stabilizing effect. In our experiment, surfactant concentration at 0.5% (w/v) of the total solution was found to be adequate.

4. Superporous hydrogels made of proteins

Proteins do not have vinyl group. Its polymerization can not be catalyzed by chemical initiator. However, proteins have free amine groups which can be crosslinked by glutaraldehyde. Therefore, superporous protein hydrogels can still be made by the gas blowing method. Superporous gelatin hydrogels were made as an example.

C. Superporous Hydrogels Prepared in Organic Solvent

Relatively hydrophobic monomers such as 2-hydroxypropyl methacrylate (HPMA) and some of the modified sucrose monomers (4) do not dissolve in aqueous solution. Organic solvents need to be used to make their superporous hydrogels. Dimethyl sulfoxide (DMSO) (Fisher Scientific) was the solvent used to make superporous hydrogels from modified sucrose monomers (4), and isopropanol was used for making PHPMA superporous hydrogel. A proper solvent should accommodate the solubility of monomer, crosslinker, foaming agent, foam stabilizer, and initiator. Bis, a crosslinker, is soluble in both isopropanol and DMSO. In DMSO, $NaHCO_3$ did not generate gas bubbles when mixed with acrylic acid, acetic acid, HCl, or citric acid. It was found that $NaHCO_3$ becomes a good gas foaming agent in DMSO or isopropanol when mixed with *p*-tolunenesulfonic acid, a strong organic acid. As described in the earlier section, PF127 was an excellent foam stabilizer for most of the hydrophilic monomers in aqueous solution. For relatively hydrophobic monomers or in organic solvent, PF127 alone did not provide a good foam stabilizing effect. However, proper combination of PF127, PP105, and SL7605 provided a satisfactory foam stabilizing effect. In this study, the APS/TEMED system was used as the initiators. However, Wako chemical company has a series of azo initiators with different decomposition rates and different solubility in organic solvent. Some of them may be better candidates than APS/TEMED for the preparation of hydrophobic superporous hydrogels in organic solvent.

All the hydrophobic superporous hydrogels did not show significant swelling in water as expected. They are most suitable for improving the mechanical strength of the hydrophilic superporous hydrogels by making interpenetrating networks. Hydrophobic monomers can also be made into copolymers with hydrophilic monomers before synthesizing superporous hydrogels.

D. Examples of Preparation of Superporous Hydrogels and Superporous Hydrogel Composites

The followings describe examples of preparation of superporous hydrogels. The structures of monomers used in our study are listed in Table 1.

Example 1. Polyacrylamide superporous hydrogel

The following components were added sequentially to a test tube (20 mm outer diameter x 150 mm in length): 1000 μl of 50% AM; 200 μl of 2.5% Bis; 460 μl of distilled deionized water (DDW); 100 μl of 10% Pluronic® F127; 25 μl of AA; 40 μl of 20% APS; and 40 μl of 20% TEMED. The test tube was shaken to mix the solution after each ingredient

spatula for 5~10 sec to accelerate foaming and to evenly distribute the gas bubbles. The gelling started within 1~2 minutes of adding $NaHCO_3$.

Example 2. Poly(sodium acrylate-co-acrylic acid) superporous hydrogel

The monomer solution was prepared by partially neutralizing acrylic acid with NaOH solution to make the final pH of 6 and the final monomer solution equivalent to 6 M of total acrylic acid and acrylate.

The following components were added sequentially to a test tube (20 mm outer diameter x 150 mm in length): 1000 µl of monomer solution; 200 µl of 2.5% Bis; 460 µl of distilled water; 100 µl of 10% Pluronic® F127; 25 µl of AA; 40 µl of 20% APS; and 40 µl of 20% TEMED. The test tube was shaken to mix the solution after each ingredient was added. Finally 90 mg of $NaHCO_3$ was added, and the whole solution was stirred vigorously using a spatula for 5~10 sec to accelerate foaming and to evenly distribute the gas bubbles. The gelling started within 1~2 minutes.

Example 3. Poly(2-hydroxyethyl methacrylate) (PHEMA) superporous hydrogel

Because hydroxyethyl methacrylate (HEMA) has slower polymerization rate than those acrylate monomers used in Examples 1 and 2, higher temperature (63°C) was used to promote the polymerization rate.

700 µl of HEMA, 100 µl of 2.5% Bis, and 100 µl of 10% Pluronic® F127 were added to a test tube (13 mm diameter x 100 mm length), and the whole solution was warmed to 63°C. To this solution were added 50 µl of 20% APS and 50 µl of 20% TEMED. After maintaining the temperature at 63°C for 80 sec, 80 mg of $NaHCO_3$ was added and vigorously stirred using a spatula for 5~10 sec to accelerate foaming and to evenly distribute the gas bubbles. The gelling started within 1~2 minutes of adding $NaHCO_3$.

In this formulation, no acid was added. Gas bubbles were generated when $NaHCO_3$ was added after the monomer mixture had reacted for 80 seconds at 63°C. Early addition of $NaHCO_3$ did not generate gas bubbles. The reason for this is not clear. One possible reason is that the gas bubbles were generated with the decomposition of $NaHCO_3$ by the heat of polymerization. If the addition of $NaHCO_3$ was too late, the viscosity of the solution became too high for a good mixing. The result was an non-uniform superporous hydrogel with low porosity. When $NaHCO_3$ was added after the start of gelling, no foam was generated at all.

Example 4. Poly(3-sulfopropyl acrylate, potassium salt) (PSPAK) superporous hydrogel

The following components were added sequentially to a test tube (13 mm outer diameter x 100 mm length): 1000 µl of 30% SPAK; 40 µl of 2.5% Bis; 50 µl of 10% Pluronic® F127; 25 µl of AA; 20 µl of 20% APS; and 20 µl of 20% TEMED. The test tube was shaken to mix the solution after each ingredient was added. Finally 90 mg of $NaHCO_3$ was added, and the whole solution was stirred vigorously using a spatula for 5~10 sec to accelerate foaming and to evenly distribute the gas bubbles. PSPAK is a strong anionic polyelectrolyte, and is charged even under acidic pH.

Example 5. Poly{2-(acryloyloxy)ethyl trimethylammonium methyl sulfate} (PATMS) superporous hydrogel

The following components were added sequentially to a test tube (13 mm outer diameter x 100 mm length): 1000 μl of 30% ATMS; 40 μl of 2.5% Bis; 50 μl of 10% Pluronic® F127; 25 μl of AA; 20 μl of 20% APS; and 20 μl of 20% TEMED. The test tube was shaken to mix the solution after each ingredient was added. Finally 90 mg of $NaHCO_3$ was added, and the whole solution was stirred vigorously using a spatula for 5~10 sec to accelerate foaming and to evenly distribute the gas bubbles.

Example 6. Poly(2-acrylamido-2-methyl-1-propanesulfonic acid) (PAMPS) superporous hydrogel

The monomer solution was prepared by partially neutralizing AMPS with NaOH solution to make the final pH at 5 and the final monomer solution at 30% (w/w).

The following components were added sequentially to a test tube (13 mm outer diameter x 100 mm length): 1000 μl of partially neutralized monomer solution; 40 μl of 2.5% Bis; 50 μl of 10% Pluronic® F127; 25 μl of AA; 20 μl of 20% APS; and 20 μl of 20% TEMED. The test tube was shaken to mix the solution after each ingredient was added. Finally 90 mg of $NaHCO_3$ was added, and the whole solution was stirred vigorously using a spatula for 5~10 sec to accelerate foaming and to evenly distribute the gas bubbles.

Example 7. Poly(N-vinyl pyrrolidinone) (PVP) superporous hydrogel

The polymerization rate of 1-vinyl-2-pyrrolidinone (VP) is slower than that of acrylate or methacrylate monomer. The APS/TEMED initiators were not effective in initiating polymerization of VP monomer even at 60°C for several hours. It was observed, however, that V545 (an azo-initiator from Wako Pure Chemical Industries, LTD, Japan.) initiated polymerization of VP monomer in less than a minute at 60°C. Since fast gelling was required for the superporous hydrogel preparation, V545 was used as the initiator in the PVP superporous hydrogel preparation.

The following components were added sequentially to a test tube (13 mm outer diameter x 100 mm length): 500 μl of VP; 200 μl of 2.5% Bis; 100 μl of water; 50 μl of 10% Pluronic® F127; and 20 μl of AA. The test tube was shaken to mix the solution after each ingredient was added. After warming in a 85°C water bath for 2 min, 50 μl of freshly made 10% V545 was added and mixed again. Immediately, 20 mg of $NaHCO_3$ was added and the whole solution was stirred vigorously using a spatula for 5~10 sec to evenly distribute the gas bubbles. The solution was kept at 85°C for 5 minutes.

At 85°C, the polymerization of VP proceeded very fast, and the gelling started within 1 minute after the addition of V545. Unlike the redox APS/TEMED initiators used in other Examples 1-6, the radical generation in this formulation was based on the thermo-decomposition of V545. Thus, the polymerization was not a pH dependent process. Since the trigger system provided by acid/$NaHCO_3$ did not exist in this formula, more accurate timing control was required to make PVP superporous hydrogels. $NaHCO_3$ should be added right after the addition of V545. Since the polymerization initiated by V545 is not pH dependent, it provides an advantage to make superporous hydrogels directly from acidic monomers (without neutralization). One example is given in Example 8.

Example 8. Poly(acrylic acid) (PAA) superporous hydrogel

In Example 2, to make superporous hydrogels from acrylic acid, the acidic monomer, acrylic acid, had to be neutralized first. Otherwise, the pH of the monomer solution would be too low, and thus the polymerization rate would be too slow when APS/TEMED were used as initiators. However, since V545 was able to initiate the polymerization even at an acidic condition, PAA superporous hydrogels could be made without the neutralization step.

The following components were added sequentially to a test tube (13 mm outer diameter x 100 mm length): 500 µl of AA; 200 µl of 2.5% Bis; 500 µl of water; 100 µl of 10% Pluronic® F127. The test tube was shaken to mix the solution after each ingredient was added. After warming in a 85°C water bath for 2 min, 100 µl of 10% V545 was added and mixed again. Within 15 sec after the addition of V545, 15 mg of $NaHCO_3$ was added and the whole solution was stirred vigorously using a spatula for 5~10 sec to evenly distribute the gas bubbles. The solution was kept at room temperature for 5 minutes.

Example 9. Poly(acrylic acid-co-acrylamide) (poly(AA-co-AM)) superporous hydrogel

The monomer mixture was prepared by adding 13 ml of AA, 9.6 g of AM, 5.81 ml of 2.5% Bis, approximately 6 g of NaOH (to adjust the final pH to about 5.1) and water to make the final volume of 100 ml.

The superporous hydrogels were prepared in a plastic test tube (17 mm in diameter x 100 mm in length) by mixing 1.5 ml of monomers, 100 µl of 10% PF127, 50 µl of 20% APS, 50 µl of 20% TEMED, and water (to make the final volume of 2 ml). The test tube was shaken to mix the solution after each ingredient was added. Finally 120 mg of $NaHCO_3$ was added, and the whole solution was vigorously stirred using a spatula for 10 sec to accelerate foaming and to evenly distribute the gas bubbles. The superporous hydrogel was then cured at room temperature for 10 min. The final monomer concentration in this preparation was about 17.4% (w/v) and the Bis concentration was 0.3 mol% of the total monomers. The foam heights in the test tubes (17 mm outer diameter) right after gelling ranged from 6.5 cm to 7 cm.

Example 10. Poly(AM-co-SPAK) superporous hydrogel

Poly(AM-co-SPAK) superporous hydrogel was prepared in an glass test tube (outer diameter of 22 mm, inner diameter of 19 mm, and height of 175 mm). The following components were added sequentially to the test tube: 1,200 µl of 50% acrylamide (AM); 900 µl of 50% 3-sulfopropyl acrylate potassium salt (SPAK); 450 µl of 2.5% Bis; 90 µl of 10% Pluronic® F127; 30 µl of 50% (v/v) acrylic acid; 45 µl of 20% ammonium persulfate. The test tube was shaken to mix the solution after each ingredient was added. Then 270 mg Ac-Di-Sol® powder was added to the mixture and stirred using a spatula to mix them. After this, 45 µl of 20% TEMED was added to the mixture and the test tube was shaken again to mix it. Finally, 100 mg of $NaHCO_3$ powder was added and the mixture was immediately stirred vigorously using a spatula for 10 sec. The superporous hydrogel was cured at room temperature for 10 min. Then the superporous hydrogel was retrieved (pinched) from the test tube using two spatulas, and washed in 1 liter beaker containing 400 ml simulated gastric fluid (SGF,

pH 1.2 based on USP) for 24 h. This step was called acidification. After this, the superporous hydrogel was dried at room temperature for 5 days.

Example 11. Poly(N-isopropyl acrylamide-co-acrylamide) (poly(NIPAM-co-AM)) superporous hydrogels

Three types of poly(NIPAM-co-AM) superporous hydrogels were synthesized. The molar ratios of NIPAM to AM in these superporous hydrogels were 9:1, 8:2, and 7:3, and the superporous hydrogels were labeled for convenience as N90, N80, and N70, respectively. The superporous hydrogels were prepared in a glass test tube (20 mm in diameter x 150 mm in length). The total monomer concentration was 1.34 M, and the total solution was 1.66 ml. The concentration of Bis, a crosslinker, was 1 mol% of the total monomer.

Monomers, crosslinker (3.43 mg of Bis), foam stabilizers, 6 N HCl (50 μl), and initiators (10 mg each of APS and TEMED) were added and mixed sequentially in a test tube. $NaHCO_3$ (60 mg) was added last, and the mixture was vigorously stirred using a spatula to accelerate foaming and to evenly distribute the gas bubbles.

For the sample N90, both PF127 (10 mg) and Silwet® 7605 (SL7605) (3 mg) were used as foam stabilizers. SL7605 was first dissolved in dimethyl sulfoxide to make a 10% solution. When only one surfactant, either PF127 or SL7605, was used for the sample N90, the foam did not stay long enough to make a uniform hydrogel foam. For the samples N80 and N70, however, only 10 mg of PF127 was used as the foam stabilizer, since PF127 alone stabilized the foam quite well due to the increased hydrophilicity by higher amount of AM.

Example 12. Superporous hydrogel containing Ac-Di-Sol®

Superporous hydrogels containing Ac-Di-Sol® was made by adding Ac-Di-Sol® to the formulation in Example 9. Before the addition of TEMED, 50~200 mg of Ac-Di-Sol® powder was added to the solution and the mixture was stirred using a spatula to evenly distribute Ac-Di-Sol®. Ac-Di-Sol® swelled in the solution and made the solution viscous. After TEMED and $NaHCO_3$ were added, the mixture was stirred vigorously using a spatula for 10 sec to accelerate foaming and to evenly distribute Ac-Di-Sol® and the gas bubbles.

Example 13. Superporous hydrogel containing Primojel®

To make the superporous hydrogels containing Primojel®, the following components were added sequentially to a glass test tube (20 mm outer diameter x 150 mm length): 600 μl of 50% AM; 120 μl of 2.5% Bis; 100 mg Primojel®; 240 μl of 10% Pluronic® F127; 700 μl of DDW; 100 μl of 6N HCl; 70 μl of 20% APS; and 70 μl of 20% TEMED. The test tube was stirred using a spatula to mix the solution after each ingredient was added. Finally 100 mg of $NaHCO_3$ was added, and the whole solution was stirred vigorously using a spatula for 5~10 sec to accelerate foaming and to evenly distribute the gas bubbles.

Example 14. Gelatin superporous hydrogel

The following components were added to a test tube (13 mm outer diameter x 100 mm length): 1 ml of 10% gelatin; 50 μl of 15 % $MgCl_2$; 20 μl of 50% (v/v) AA. After the mixture was warmed to 85°C, 40 μl of 6% glutaraldehyde and a suspension containing 15 mg of $NaHCO_3$ were added, and the whole solution was stirred vigorously using a spatula for 5~10 sec and left at 85°C for 10 min.

For the preparation of gelatin superporous hydrogels, glutaraldehyde was used as a cross-linker. $MgCl_2$ was the catalyst for polymerization. Gelatin concentration higher than 10% is not recommended because the viscosity becomes too high for good mixing. Since the crosslinking reaction was too slow at room temperature, 85°C was used to accelerate the crosslinking reaction. No surfactant was needed because gelatin itself acted as a surfactant in this formulation. 15 mg $NaHCO_3$ was first mixed with 15 μl of water to make a suspension before it was added to the solution. This was because $NaHCO_3$ in the suspension state could be mixed faster in the solution than $NaHCO_3$ in the dry state. Unlike the superporous hydrogels made from the acrylate monomers, the gelatin foam collapsed after it was cured.

Example 15. Poly(2-hydroxypropyl methacrylate) (PHPMA) superporous hydrogel

The following components were added sequentially to a test tube (13 mm outer diameter x 100 mm in length): 500 μl of HPMA ; 200 μl of 10% Bis (in DMSO); 90 μl of 10% Silwet® L7605 (in DMSO); and 30 μl of 5% Pluronic® P105 (in DMSO). The test tube was shaken to mix the solution after each ingredient was added. After warming in a 80°C water bath, 180 μl of 10% APS (in water) and 90 μl of 10% TEMED (in water) were added and mixed again. After 30 sec at 80°C, 30 mg of $NaHCO_3$ was added and the whole solution was stirred vigorously using a spatula for 5~10 sec. In the above formulation, 500 μl of HPMA can be replaced with 500 μl of 50% HPMA in isopropanol.

In the above experiments, no acid was added. Gas bubbles were generated when $NaHCO_3$ was added after the monomer mixture had reacted for 30 seconds at 80°C. Addition of $NaHCO_3$ prior to 30 seconds did not generate gas bubbles. The reason for this is not clear, but one possible reason is that the gas bubbles were generated with the decomposition of $NaHCO_3$ by the heat of the polymerization. The combination of the two foam stabilizers was important, since any one of them alone did not provide a good foam stabilizing effect.

Example 16. Superporous hydrogels with mucin coating on the surface

Another important property of the superporous hydrogels useful in many applications is slipperiness of the surface. The surface of superporous hydrogels was modified with mucin (Sigma Chemical Company, type II, crude) to increase the surface slipperiness.

The superporous hydrogels prepared in Example 10 (poly(AM-co-SPAK) superporous hydrogels) were acidified and dried. The rough side (i.e., the side that did not face the glass test tube during synthesis) was trimmed to remove the rough surface. The superporous hydrogels were then coated with 10% mucin solution (Sigma Chemical Company, type II, crude) using a cotton Q-tip. The coated superporous hydrogels were heated in 130°C oven for 40 min. This coating and heating processes were repeated twice more.

Heating albumin emulsion at 100~160°C has been used to make crosslinked albumin microspheres (29). At high temperature, protein forms crosslinked networks. At 130°C, mucin also crosslinked on the surface of the superporous hydrogels. The slipperiness was kept even the coated superporous hydrogels were washed in SGF for more than two days. On the other hand, if the mucin-coated superporous hydrogels were not heated but dried at room temperature, the slipperiness was maintained for only one hour because the surface mucin was not crosslinked and was dissolved in SGF.

IV. CHARACTERIZATION OF SWELLING KINETICS AND EXTENT OF SUPERPOROUS HYDROGELS

A. Fast Swelling of Superporous Hydrogels

According to the kinetics of the swelling of a gel (30), the characteristic time of swelling (τ) is proportional to the square of the characteristic length of the gel (L) and is inversely proportional to the diffusion coefficient of the gel network in the solvent (D) as follows:

$$\tau = L^2/D$$

The characteristic length for a spherical hydrogel is the radius, and for a hydrogel sheet is the thickness. The diffusion coefficient of hydrogel networks is in the order of 10^{-7} cm^2/sec (24,30). A 1 mm-thick gel slab with a diffusion coefficient of 10^{-7} cm^2/sec will take over an hour to reach 50% of the equilibrium swelling and more than six hours to reach 90% of equilibrium (31). This is far too slow for the gels to be used in practical applications, such as superabsorbents in baby diapers. To make fast swelling superabsorbent polymers (SAPs), submillimeter size gels in a powder form are commonly used in industry. The restriction on the size of the gels limits useful application of the SAP, and certainly SAP with larger dimension would be highly desirable (32).

The total swelling time for a dried superporous hydrogel in aqueous solution is determined by two factors: t_1 and t_2. t_1 is the time for water to reach all the surface of the pores in the superporous hydrogels. It is determined by the effectiveness of the capillary action in a superporous hydrogel. t_2 is the actual swelling time of the polymer matrix which is determined by the thicknesses of the cell walls and struts. Because the thicknesses of the cell wall and strut of superporous hydrogels are very thin, ranging from less than a micrometer to tens of micrometers, they have a very short characteristic swelling time. For superporous hydrogels, t_2 is comparable to that of a ultra-thin hydrogel film. The capillary action is mainly determined by the availability of capillary channels and the wettability of the channels. Various approaches have been attempted to maintain good capillary action (i.e., to decrease t_1) by maintaining open intercellular channels and good surface wettability.

B. Density and Swelling Ratio Measurement

Partially neutralized acrylic acid (AA) and acrylamide (AM) were used as monomers. The degree of neutralization of AA by NaOH was 70% to 100%. The molar ratio of AA to AM was 5:4. Bis was used as a crosslinker and its concentration was 0.3 mol% of the total monomer. These numbers were chosen according to one formula used in the diaper industry (33). The poly(acrylic acid-co-acrylamide) (poly(AA-co-

AM)) superporous hydrogels were prepared according to Example 9. The final monomer concentration in this preparation was about 17.4% (w/v) and the Bis concentration was 0.3 mol% of the total monomers.

After the superporous hydrogels were prepared, they were treated by different processes. The effects of these processes on the density, swelling ratio, and swelling time of superporous hydrogels were studied. In addition, effects of different additives on the swelling properties of superporous hydrogels were examined (Table 2).

The density (d) of the dried superporous hydrogels was calculated by: $d = W_d/V_d$, where W_d is the weight of a dried superporous hydrogel and V_d is the volume of the dried superporous hydrogel. Since some of the dried superporous hydrogels lost their cylindrical shape after drying, direct measurement of their volumes was difficult. V_d was determined by a solvent displacing method. Briefly, a dried superporous hydrogel was forced to submerge underneath the surface of hexane in a graduate cylinder using tweezers and then was quickly removed from hexane. The volume change read from the graduate cylinder before and after the removal was the volume of the dried superporous hydrogel. The accuracy of this method is about the same as using ruler to measure the diameter and length of a regularly shaped superporous hydrogels. Hexane was used in our study because it was very hydrophobic so that the superporous hydrogels did not swell and absorb the solvent.

For the swelling study, deionized distilled water (DDW) was used as the swelling medium. Each superporous hydrogel was cut into disk shape with the diameter about twice as much as the height (for instance, Sample #4 in Table 2 had diameter of 0.8 cm and height of 0.4 cm) and weight ranging from 50 mg to 65 mg. Since superporous hydrogels became too fragile to handle after swollen, the swelling ratio Q was determined by the sieve method. The swelling ratio, Q, is defined as:

$$Q = (W_s - W_d)/W_d$$

where W_s is the weight of the swollen superporous hydrogel and W_d is the weight of the dried superporous hydrogel. A superporous hydrogel was placed on a sieve weighing boat. The sieve weighing boat containing the superporous hydrogel was immersed in DDW to let the superporous hydrogel swell to equilibrium. To measure Q, the boat was taken out to drain the free water from the sieve and paper towel was used to remove excess water from underneath the sieve. Then the weight of the swollen superporous hydrogels was measured by subtracting the boat weight from the whole weight. This method avoided the direct handling of the fragile superporous hydrogels.

The swelling time is the time for a superporous hydrogel to reach the equilibrium swollen state when placed in the swelling medium, DDW. All the data in Table 2 were based on at least 3 samples.

C. Comparison of Non-porous Hydrogels and Superporous Hydrogels

Non-porous hydrogels (Sample #1 in Table 2) were prepared by the same formula used for superporous hydrogel preparation except no PF127 and $NaHCO_3$ were added. Sample #2 was prepared based on the formula described in Example 9. After polymerization, superporous hydrogels were retrieved using a spatula from the test tube and dried in a 55°C oven for a day. In Sample #3, the retrieved superporous hydrogels were allowed to swell in DDW to equilibrium and washed several times in

DDW. Then the washed superporous hydrogels were dried in 55°C oven for a day. This step removed the water-soluble components remaining in the superporous hydrogels such as foam stabilizer PF127. The absence of such water-soluble components is expected to affect the extent of collapse of the superporous hydrogels during drying due to the increased surface tension to that of pure water.

Due to the porous structures, Samples #2 and #3 had density of 0.76 and 0.80 g/cm^3, respectively, which were smaller than that of the non-porous gels (1.30 g/cm^3). Samples #2 and #3 also had higher swelling ratios (Q = 328 and 307, respectively) than that of hydrogels (Q = 173). Again, this was due to the porous structures of superporous hydrogels. Water could be hold in the open pores so that the overall water absorbency was higher for the superporous hydrogels. Samples #2 and #3 swelled much faster (31 min and 51 min, respectively) than the non-porous hydrogels (720 min). Sample #3 had longer swelling time than Sample #2. The possible reason is the wettability difference in Samples #2 and #3. Since Sample #2 was not washed, there were water soluble ingredients, such as PF127, left on the surface of the superporous hydrogels. These ingredients might have changed the wettability so that Sample #2 swelled faster than Sample #3.

Although the superporous hydrogels in Samples #2 and #3 swelled much faster than the conventional, non-porous hydrogels, their swelling time was still far slower than our expectation. The time-limiting step for the swelling of these superporous hydrogels was found to be the water penetrating step (i.e., t_1). It took almost all the swelling time for water to reach the center of a superporous hydrogel. After the water reached the center of the superporous hydrogels, they quickly swelled to their equilibrium sizes. This meant t_2 was very short in the superporous hydrogel, but t_1 was very long. To decrease the total swelling time, t_1 must be deceased. Therefore, our subsequent effort was focused on the ways to accelerate the water penetration by improving the capillary action.

D. Effect of Ethanol Dehydration on the Swelling Kinetics of Superporous Hydrogels

Sample #2 of Table 2, which are the superporous hydrogels dried in an oven without washing after the synthesis, took more than 30 min for equilibrium swelling. This rather slow swelling originated from the drying process. The synthesized superporous hydrogel contained water which was present in the monomer mixture (the concentration of monomer was 17.4% (w/v)). During the drying process, the individual polymer chains were brought together due to the high surface tension of water (72 dyn/cm at room temperature), and this action closed some of the pores. As a result, the foam shrank to a smaller and more condensed piece (density of 0.76 g/cm^3). Many of the capillary channels were closed or partially blocked to form "dead end" structures. Thus, no capillary action is expected even in contact with water. Therefore, the penetration of water to the center of the superporous hydrogel was very slow. It was found that ethanol dehydration was a good approach to solve the problem associated with the air drying process.

To prepared Sample #4, the synthesized superporous hydrogels were dehydrated using absolute ethanol. After a superporous hydrogel was synthesized in a test tube, 5~10 ml of absolute ethanol was added to the test tube to dehydrate the superporous hydrogel. After the initial dehydration step (during which some water was replaced by ethanol), the superporous hydrogel was retrieved and further dehydrated in a plate containing 50 ml of absolute ethanol several times to ensure replacement of all the water by ethanol. During the dehydration process, the soft and flexible

superporous hydrogels became hard and brittle. After the dehydration was completed, the excess ethanol in dehydrated superporous hydrogels was removed by draining using paper towel. Then the superporous hydrogels were dried in a 55°C oven for a day. For Sample #5, the synthesized superporous hydrogels were first allowed to swell to equilibrium in DDW before dehydrated using absolute ethanol.

The ethanol-dried superporous hydrogels without preswelling in DDW (Sample #4) had density of 0.26 g/cm^3, which is much lower than that of Sample #2 (0.76 g/cm^3). This means that the ethanol dehydrated superporous hydrogels had much higher porosity. The swelling ratio of Sample #4 was similar to that of Sample #2, indicating that dehydration did not change the water absorbency. The swelling time, however, was greatly decreased in Sample #4 (4.8 min in Sample #4 vs. 31 min in Sample #2).

The major factor that contributes to the fast swelling of ethanol dehydrated superporous hydrogel is the preserved capillary channels. Because ethanol is a non-solvent to the polymer, during the dehydration process, water was replaced by ethanol, and consequently the polymer chains were precipitated from the ethanol and lost their flexibility. This is why the superporous hydrogels became hardened after the dehydration. When the dehydrated superporous hydrogels were dried in 55°C oven, because the polymer chains could not move freely, they could not be brought together by the low surface tension of ethanol. Therefore, the superporous hydrogels did not collapse and thus the capillary channels were preserved after the drying process. Ethanol has low surface tension (22 dyn/cm compared with 72 dyn/cm of water at room temperature), which means the driving force for the collapse of the polymer network is smaller. For the dehydration process, not only ethanol, but other organic solvents such as acetone, methanol, and isopropanol, etc., can also be used.

Superporous hydrogels dehydrated by ethanol had larger pore size and lower density than those without ethanol dehydration. SEM pictures showed that the number and the size of pores of Sample #4 were much greater than those of Sample #2. Also the pores in Sample #4 were interconnected to form capillary channels so that water could easily penetrate to the center of the superporous hydrogels. Similar structural differences can also be found in sucrose superporous hydrogels prepared with and without ethanol dehydration.

In Sample #5, the superporous hydrogels were swollen in DDW before dehydration with ethanol. Superporous hydrogels of Sample #5 had a density of 0.13 g/cm^3, which is even lower than 0.26 g/cm^3 of Sample #4. This is because in Sample #5, the superporous hydrogels were fully swollen before the dehydration, i.e., polymer chains were fully relaxed. Dehydration under this state resulted in a superporous hydrogel with larger volume. Lower density in Sample #5 suggested that they had even better capillary system. This contributed to the slightly faster swelling time in Sample #5 (4.1 min) than Sample #4 (4.8 min).

In plastic foams, such as a phenolic foam, the most common type of pores are several hundred micrometers. Shutov found that, in addition to those large pores (which were called macrocells), there were secondary pores with diameters about 1 μm (which were called microcells) in the wall of the macrocells (34). The presence of microcells was also found in our superporous hydrogels. The size of the microcells were 0.1 to 5 micrometers as measured from the SEM pictures. The microcells were two or three orders of magnitude smaller than the main pores of the superporous hydrogels.

E. Effect of Wetting Agent on the Swelling Kinetics of Superporous Hydrogels

The mere presence of interconnected capillary channels is not enough for a good capillary action. The surface of the superporous hydrogels must also have good wettability. Both samples #4 and #5 in Table 2 had good capillary channels, but the water penetration still took more than 4 min. The major reason for this was that the surface of superporous hydrogels did not have good wettability. The surface wettability is mainly determined by the type and properties of polymers, the surface roughness, and the swelling medium. Since the surface roughness at the microscopic level is not easy to control, and the most useful medium is water, we have changed the surface properties of the superporous hydrogel using different wetting agents.

Wetting agents change the surface wettability. Kellenberger et al. (35) used Voranol® (a polyol made by Dow Chemical Company) as a wetting agent to increase the swelling rate of polyacrylate hydrogel particles. In our study, Sample #6 was made by dehydrating the superporous hydrogels with ethanol containing 1% $\text{Voranol}_{240\text{-}800}$® (the numbers indicated in Voranol are related to the hydroxy number and the molecular weight). As shown in Table 2, Sample #6 treated with Voranol had the similar density and swelling ratio to those of Sample #4. However, Sample #6 had faster swelling time (t = 2.8 min) than Sample #4 had (t = 4.8 min). This study showed that the wetting agent could decrease the swelling time by providing better surface wettability. $\text{Voranol}_{240\text{-}800}$® was used just as an example. It decreased the swelling time by almost two minutes. It is possible that other wetting agents could decrease the swelling time even more. More study is needed to examine other wetting agents.

F. Effect of Moisture Contents on the Swelling Kinetics of Superporous Hydrogels

Samples #7 and #8 in Table 2 were prepared by moistening Sample #2 and 4, respectively. A dried superporous hydrogel was placed on a support which was placed in a covered container with a small amount of water at the bottom (Fig. 3). This device constituted a moisture chamber. Sample #7 was made by placing Sample #2 in the moisture chamber for 24 h at room temperature. The superporous hydrogels absorbed 126 ± 11% of its original weight moisture. Sample #8 was made by placing Sample #4 in the moisture chamber for 12 h at room temperature. It absorbed 81 ± 4% of its original weight moisture. The amount of moisture absorbed was controlled by the length and the temperature of moistening.

The swelling ratio did not change after moisturization. All four samples (Sample #2, 4, 7, 8) had similar swelling ratios in DDW (Table 2). However, moistening significantly decreased the swelling time. After this treatment, the swelling time of Sample #7 decreased from 31 min (of Sample #2) to only 7 min, while the swelling time of Sample #8 decreased from 4.8 min (of Sample #4) to only 37 sec.

As previously discussed, the water penetration step is the time-limiting step for the swelling of superporous hydrogels. The deceased swelling time after moistening is thought to be caused by the improved surface wettability of the superporous hydrogels. Sample #2 had poor capillary channels and poor wettability. It took 31 min for equilibrium swelling. Sample #7 had poor capillary channels but better wettability so that the swelling was decreased to 7 min. Sample #4 had good capillary

channels but poor wettability. Its swelling took 4.8 min. Sample #6 had good capillary channels and good wettability and its swelling was completed in only 37 sec.

The change of surface wettability after moistening is caused by the amphiphilic property of the hydrogels. The polymer chains in the hydrated state had high mobility. When a superporous hydrogel was dried, the polymer chains at the air-polymer interface changed their orientation and/or conformation to decrease the free energy so that the relatively hydrophobic side chains or backbones faced the air. This led to the change of surface character from relatively hydrophilic to relatively hydrophobic. During the moistening treatment, this process reversed. The polymer chains changed their orientation and/or conformation again and the surface character became relatively hydrophilic (36,37) This change caused the improved wettability in Sample #7 and 8.

G. Effect of Superdisintegrants on the Swelling Kinetics of Superporous Hydrogels

Ethanol dehydration of superporous hydrogels significantly decreases the swelling time. This process, however, requires repetitive use of ethanol to complete dehydration. In an attempt to find a simpler approach, we tried to incorporate superdisintegrants into the superporous hydrogels.

Superdisintegrants, such as Ac-Di-Sol®, Primojel®, Explotab®, and Crospovidone® have been used extensively in tablets and capsules to promote their fast disintegration. The mechanism of disintegration is based on swelling, wicking, and deformation of the disintegrants (38). When a compressed tablet is placed in aqueous solution, water can be quickly absorbed, and the swelling of the disintegrants breaks apart tablets quickly. As mentioned above, the air dried superporous hydrogels lost the interconnected capillary channels (Sample #2 in Table 2). In the presence of incorporated superdisintegrants, however, the "dead-ended" structures in the collapsed superporous hydrogels can be expanded by the swelling of the incorporated superdisintegrants and the collapsed channels can be opened up to recover the capillary action.

1. Effect of crosslinked sodium carboxymethylcellulose (Ac-Di-Sol®)

Ac-Di-Sol® (FMC Corporation) is a crosslinked sodium carboxymethylcellulose. In the dry state, it exists as stiff fibers with diameter of 10~20 μm and length of 100~200 μm. To be incorporated in Sample #9~12 in Table 2, various amounts (50 mg ~ 200 mg) of Ac-Di-Sol® were added to the monomer solution before the addition of TEMED. The solution was stirred using a spatula to evenly distribute Ac-Di-Sol® so that a viscous mixture was formed. The stirring after the addition of $NaHCO_3$ further mixed Ac-di-sol®, and after the beginning of polymerization by addition of $NaHCO_3$, the viscosity increased quickly and the sedimentation of Ac-di-sol® to the bottom of the tube was negligible. After the polymerization was complete, the superporous hydrogels were dried in 55°C oven for a day.

Samples #9, #10, #11, and #12 in Table 2 had densities of 0.48, 0.39, 0.33, and 0.28 g/cm^3, respectively. The increase in the Ac-Di-Sol® content decreased the density of the synthesized superporous hydrogels. When Ac-Di-Sol® was mixed with the monomer solution, it swelled so that monomers (AM and AA) and crosslinker (Bis)

were absorbed into the cellulose network. After polymerization is complete, the cellulose network of an Ac-Di-Sol® particulate and the crosslinked poly(AA-co-AM) network formed an interpenetrating polymer network (IPN). This IPN formation is limited to the Ac-Di-Sol® particulate, and thus the localized IPNs (or Ac-Di-Sol® particulate) basically function as a crosslinker of the synthesized superporous hydrogels. During the drying process, the rigid Ac-Di-Sol® fibers maintained the network structure so that the superporous hydrogels shrank less. The superporous hydrogels with higher Ac-Di-Sol® content had higher porosity and better capillary channels.

The addition of Ac-Di-Sol®, however, decreased the swelling ratio of the superporous hydrogels. The swelling ratio of Sample #2, 9, 10, 11, and 12 were 328, 294, 192, 120, and 91, respectively. The decrease was due to the increase in crosslinking by the localized IPNs. On the other hand, the addition of Ac-Di-Sol® dramatically decreased the swelling time. The swelling time of Sample #2, 9, 10, 11, and 12 were 31 min, 8.5 min, 1.2 min, 35 sec, and 22 sec, respectively.

The function of Ac-Di-Sol® in promoting the swelling speed was two-folds. First, it helped retain the capillary channels. This is evident from the lower density of superporous hydrogels incorporated with Ac-Di-Sol®. However, when compared with Samples #4, #5, and #6, Sample #12 had higher density but shorter swelling time. This suggested that the retained capillary channels was not the only reason for its fast swelling. It is thought that another contribution of Ac-Di-Sol® was its hydrophilicity. Ac-Di-Sol® has high wettability with a contact angle of 0° (39). The incorporation of Ac-Di-Sol® made the surface of superporous hydrogels more hydrophilic and have better wettability.

Compared with the ethanol dehydration process, the addition of super-disintegrants is simpler and less expensive. In addition, it has another advantage. After the addition of Ac-Di-Sol®, the monomer solution became viscous. This was good for the foam preparation because at higher viscosity foams could be stabilized longer.

2. Effect of crosslinked sodium starch glycolate (Primojel®)

The effect of Primojel® on the swelling time of superporous hydrogels was also studied. Primojel® is a cross-linked sodium starch glycolate.

Superporous hydrogel containing Primojel® was prepared based on Example 13. The superporous hydrogel was dried in 55°C oven after the synthesis. For comparison, control superporous hydrogels containing no Primojel® were also prepared. They were either dried in 55°C oven after synthesis or were dehydrated by ethanol followed by oven drying. The swelling time of these three groups of superporous hydrogels were tested in DDW. The swelling time of the superporous hydrogel containing no Primojel® and without ethanol dehydration was 8.5 min. The swelling time of the superporous hydrogel containing no Primojel® but with ethanol dehydration was 1.4 min. The swelling time of the superporous hydrogel containing 100 mg Primojel® but without ethanol dehydration was only 0.6 min. This study shows

that Primojel® can also significantly decrease the swelling time of a superporous hydrogel.

In addition to Ac-Di-Sol® and Primojel®, other tablet disintegrants such as Explotab® and Crospovidone®, have similar mechanism in tablet disintegration. As with Ac-Di-Sol®, Primojel® and Explotab® are very hydrophilic with a contact angle of 0° (39). They are also expected to have the ability to promote the swelling of superporous hydrogels.

H. Effect of Crosslinking Density on the Swelling Kinetics of Superporous Hydrogels

To study the effect of crosslinking density on the swelling properties, superporous hydrogels containing different amount of crosslinker were prepared. The crosslinker (Bis) contents in Sample #2, #13, and #14 in Table 2 were 0.3 mol%, 0.6 mol%, and 0.9 mol% of the monomer content, respectively.

Table 2 shows that the increase in the crosslinker concentration decreased the density of the superporous hydrogels (0.76, 0.45, and 0.38 g/cm^3 for Sample #2, #13, and #14, respectively). It is not surprising that the swelling ratio also decreased when more crosslinker was incorporated. It is interesting to note that when more crosslinker was used, the swelling time also decreased significantly (31 min, 13.4 min, and 3.1 min for Sample #2, #13, and #14, respectively). The faster swelling of Sample #13 and #14 is explained based on their structure observed by SEM. At higher cross-linking density, the polymer networks became more rigid. Therefore, during the drying process, the superporous hydrogels shrank less and the capillary channels were less likely blocked. The interconnected capillary channels were observed in Sample #14 while many of these channels were blocked in Sample #2.

I. Other Factors Affecting the Swelling Kinetics of Superporous Hydrogels

The type of polymer can have great impact on the swelling kinetics of superporous hydrogels. For superporous hydrogels having the same porous structures, the one with better wettability swells faster. It is believed that the main factor determining water wettability of a hydrogel is the chemical structure of the polymer network at the interface (36). Superporous hydrogels synthesized from glycidyl acrylate modified sucrose monomer swelled to equilibrium in less than 0.3 min after treated by ethanol dehydration (4), while similar size superporous hydrogels prepared by the same method (Sample #4) took 4.8 min to reach equilibrium. This difference is partially attributed by the different wettability of the polymers.

The porosity can also affect the swelling kinetics of superporous hydrogels. The porosity of superporous hydrogel is mainly determined by the amount of blowing agent added. Superporous hydrogels with higher porosity are less likely to have blocked channels. In addition, when more blowing agent is used, the superporous hydrogels have thinner cell walls which results in the shorter characteristic time t_2. Superporous hydrogels prepared with more acid had faster swelling time than those prepared with less acid.

It was suggested that the wettability of polymeric foams can be improved by washing with Span® 20 solution or $CaCl_2$ solution (40). In this study, superporous hydrogels were treated by the same processes. Such treatments, however, did not result in any improvement on the swelling kinetics of the superporous hydrogels.

V. CHARACTERIZATION OF MECHANICAL STRENGTH OF SUPERPOROUS HYDROGELS AND SUPERPOROUS HYDROGEL COMPOSITES

The high mechanical strength of superporous hydrogels is important for many applications. Quite often the mechanical strength of superporous hydrogels, as well as conventional hydrogels, is low to compromise the usefulness of the other functional properties of hydrogels and superporous hydrogels. One of the important applications of hydrogels and superporous hydrogels is in the development of oral controlled drug delivery systems. Hydrogels have been used as a platform for long-term (more than 24 h) oral drug delivery. Due to the large size and slippery surface of fully swollen hydrogels, they have been successfully used as a gastric retentive device for long-term oral drug delivery (2,3). One of the limitations of using hydrogel-based gastric retentive device was that the dried hydrogels swelled too slow so that all the dried hydrogels administered to dogs were emptied into the stomach before fully swelling to a desired size. To avoid the slow swelling problem with conventional hydrogels we synthesized fast swelling hydrogels, i.e., superporous hydrogels, as mentioned above. While the superporous hydrogels swelled very quickly regardless of the size, the mechanical strength of fully swollen superporous hydrogels was poor to be useful. Thus, we synthesized various superporous hydrogel composites to enhance the mechanical strength of the fully swollen superporous hydrogels.

The main idea of making superporous hydrogel with high mechanical strength was based on our observation. During the study on swelling kinetics of various superporous hydrogels described above (IV. Characterization of swelling kinetics and extent of superporous hydrogels), we observed that some samples of superporous hydrogels containing Ac-Di-Sol® or Primojel® maintained high mechanical strength even after equilibrium swelling. This led us to further investigation of the mechanical properties of superporous hydrogel composites. Formulation variables, such as the amount of crosslinker, amount of Ac-Di-Sol®, type and amount of plasticizer, type of monomer, amount of blowing agent as well as process variables such as acidification, all affect the mechanical properties of the superporous hydrogels.

A. Testing Method of Mechanical Properties

A bench comparator (B.C. Ames Company, Waltham, MA) was used to test the mechanical properties of the superporous hydrogels. A superporous hydrogel that was swollen in simulated gastric fluid (SGF) was placed longitudinally under the lower touch of the bench comparator that was connected to a micrometer gauge. The superporous hydrogel was supported by a lab jack. Weights were applied to the upper touch of the bench comparator in increasing amounts. The swelling height of the superporous hydrogel under pressure was read from the gauge. The pressure applied to the superporous hydrogel was calculated from the amount of weights and the contact area of the lower touch. Two parameters, swelling height under 100 cm water pressure and ultimate compression pressure (UCP), were determined to characterize the mechanical properties of the superporous hydrogels. The UCP was determined by

applying increasing amounts of weights until a point when the superporous hydrogel started cracking. The pressure at that point was defined as the UCP.

B. Effect of Ac-Di-Sol® on the Mechanical Properties of Superporous Hydrogels

The presence of Ac-Di-Sol® in superporous hydrogels is critical for the improved properties of the superporous hydrogels. As discussed above, Ac-Di-Sol® significantly improved both the swelling kinetics and the mechanical properties of superporous hydrogels. In another study, Ac-Di-Sol® was also found to significantly increase the mechanical strength of the conventional, non-porous hydrogels (see VI. Characterization of mechanical strength of hydrogel composites). The effect of Ac-Di-Sol® on the mechanical strength of superporous hydrogels was examined in more detail.

Superporous hydrogels containing different amount of Ac-Di-Sol® (0 to 300 mg) were prepared based on poly(AM-co-SPAK) (see Example 10 in Section III. D. Examples of Superporous Hydrogel Preparation) except that all these superporous hydrogels were not undergone the acidification step (i.e., they were not treated with simulated gastric fluid). The mechanical properties of these superporous hydrogels were studied on bench comparator after they swelled to the equilibrium size in SGF.

Incorporation of Ac-Di-Sol® slightly decreases the swelling size of the superporous hydrogels from 1.8 to 1.2 cm in the presence of 100 cm water pressure. On the other hand, it considerably increases the UCP value (o) of the superporous hydrogels from below 150 to about 250 cm water pressure. This is a rather dramatic increase in mechanical strength. It is thought that the addition of Ac-Di-Sol® increases the effective cross-linking density of the superporous hydrogel. This increase in effective crosslinking density is different from increasing the crosslinking density by other conventional crosslinkers such as Bis. When the concentration of Ac-Di-Sol® was too high, the viscosity of the monomer solution also became too high, and this made a good mixing of all the ingredients difficult. Thus, 270 mg Ac-Di-Sol® was used in our study.

When Ac-Di-Sol® fibers were mixed with the monomer solution, they swelled and absorbed the monomer solution. When the polymerization was initiated, the monomers inside the Ac-Di-Sol® fibers polymerized along with the bulk monomer solution so that local interpenetrating polymer networks (IPNs) around the Ac-Di-Sol® fibers were formed. Ac-Di-Sol® fibers were chemically bonded to the superporous hydrogel matrix as an integral unit. This structure allows significant increase in the overall mechanical strength of superporous hydrogels. The physical entanglements of Ac-Di-Sol® fibers with the polymer network is also confirmed by SEM (Fig. 5).

C Type of Monomer on the Mechanical Properties of Superporous Hydrogels

The type of monomer used in the superporous hydrogel preparation significantly affects the mechanical properties of the superporous hydrogels. When acrylamide (AM) was used as the only monomer, the superporous hydrogels did not show large swelling volume nor good mechanical strength. When SPAK was used alone, the superporous hydrogels swelled to a large size but were not strong. When AM and AA were copolymerized, the superporous hydrogels did not swell very large in SGF, and

also the superporous hydrogels deformed to a very small size under 100 cm water pressure. However, when AM and SPAK were copolymerized, the superporous hydrogels showed good swelling and also good mechanical properties.

D. Acidification on Mechanical Properties of Superporous Hydrogels

Various post-treatments of synthesized superporous hydrogels were attempted to improve the mechanical strength of superporous hydrogels. After the superporous hydrogels were prepared as in Example 10, they were washed in the SGF (pH 1.2) for 24 h. They were then dried in a 60°C oven or air dried at room temperature. The dried superporous hydrogels were allowed to swell in SGF and their mechanical properties were tested using the bench comparator.

Superporous hydrogels with three different post-treatments were tested: (A) superporous hydrogels without washing in SGF; (B) superporous hydrogels washed in SGF and then oven dried at 60°C for 24 h; and (C) superporous hydrogels washed in SGF and then air dried at room temperature for 5 days. The washing step partially acidified the anionic SO_3^- group into SO_3H group, and it substantially changed the properties of the superporous hydrogels. The UCP value for the three samples A, B, and C were 189, 284, and 368 cm water pressure, respectively. The acidification of the superporous hydrogels made them much stronger than the superporous hydrogels without acidification. Moreover, the UCP of the acidified superporous hydrogels that were dried at room temperature were even stronger than those dried in a 60°C oven. It is clear that acidification provided a significant improvement in the mechanical properties of superporous hydrogels.

VI. <u>CHARACTERIZATION OF MECHANICAL STRENGTH OF HYDROGEL COMPOSITES</u>

Highly swelling hydrogels usually possess weak mechanical strength and such a property limits applications of otherwise useful hydrogels. Thus, improving the mechanical properties while maintaining high swelling ratio is highly desirable even for the conventional hydrogels. Since the finding that Ac-Di-Sol® fibers increased the mechanical strength of superporous hydrogel composites, we examined the effect of Ac-Di-Sol® fibers on the mechanical strength of conventional hydrogels. It was found that when Ac-Di-Sol® fibers were used to make conventional hydrogel composites, the increase in the mechanical strength was even more significant than in the superporous hydrogels.

A. Synthesis of Hydrogel Composites

In a plastic test tube (17 mm x 100 mm), Ac-Di-Sol, AM, Bis, APS, and distilled water were sequentially added to make the final volume of 5 ml. The amount of Ac-Di-Sol was varied as listed in Table 3. The final AM concentration was 10% (w/v), and the concentration of Bis (crosslinker) was 0.46 mol% of the monomer. The concentration of APS was 4% (w/w) of the monomer, AM. The solution was then stirred to thoroughly mix all the ingredients. Then, TEMED, at the concentration of 4% (w/w) of the monomer, was added and the solution was stirred vigorously for 15 sec for further mixing. The gelling started within 30~60 sec after the addition of TEMED. The prepared hydrogels were cured at room temperature for 24 h followed by washing in distilled water for 4 days. Polyacrylamide (PAM) hydrogels containing Crospovidone XL were also synthesized in the same manner (Table 3). The contents of Ac-Di-Sol and Crospovidone XL in the dried hydrogels were calculated based on the

amount added. As a control, PAM hydrogels with different amounts of crosslinking agent were synthesized. The final monomer concentration was also 10% (w/v) for all samples, and the concentration of Bis was varied from 0.46 mol% to 1.84 mol% of the monomer.

1. Calculation of compression modulus

Fully swollen hydrogels were cut into discs with 1 cm length. Their diameter ranged from 1.2 cm to 1.8 cm. The mechanical properties were tested using a bench comparator. Briefly, a cylindrical, swollen hydrogel was placed under a plate which was connected to a micrometer gauge. Weights were applied in increasing amounts and the hydrogel deformation (i.e., the height difference between undeformed and deformed hydrogel) was recorded for each weight. After each measurement, the weights were completely removed and the hydrogel was allowed to recover to its initial height before the next weight was added. The linear portion which occurred when the deformation was less than 10% of its original height was used to calculate the force/deformation coefficient. The compression modulus was calculated by the following equations:

$$E_c = SH_s/A_s$$

where E_c is compression modulus, S is force/deformation coefficient. H_s is the height of the fully swollen gel, A_s is the area of the top of a fully swollen gel.

2. Swelling study

The washed hydrogels were air dried to a constant weight. The swelling study was conducted in distilled water at room temperature. At timed intervals, the gels were removed from water, blotted to remove excess water, and weighed. The swelling ratio Q was calculated by:

$$Q = (W_s-W_d)/W_d$$

where W_s and W_d were the weights of the swollen and dried gels, respectively.

B. Characterization of Hydrogel Composites

Fig. 6 shows changes in the swelling ratio and compression modulus of the polyacrylamide and Ac-Di-Sol composites as a function of the Ac-Di-Sol content. When the Ac-Di-Sol content increased from 0% to 50% of the total weight of the dried hydrogel, the compression modulus (representing the resistance to pressure) increased 4.7 folds from 0.25 to 1.17 kg/cm^2 (Fig. 6-A) and the swelling ratio decreased 2.4 folds almost linearly from 19.0 to 7.8 (Fig. 6-B). The decrease in the equilibrium swelling ratio is understandable since the individual Ac-Di-Sol fibers are expected to function as chemical as well as physical crosslinking agents.

The changes in the swelling ratio and compression modulus with increase in the Crospovidone XL content were similar to those in the polyacrylamide and Ac-Di-Sol composites described above. When the content of Crospovidone XL increased from 0% to 60% of the hydrogel dry weight, the compression modulus increased from 0.25 to 1.07 kg/cm^2 (4.2 folds), while the swelling ratio decreased from 19.0 to 4.3 (4.4 folds). For the conventional hydrogels using increasing amount of crosslinker such as Bis but containing no Ac-Di-Sol or Crospovidone XL, the increase in the compression modulus was small. When the Bis content increased from 0.46 mol% to

1.84 mol%, the compression modulus increased from 0.25 to 0.71 kg/cm^2 (2.8 times), and the swelling ratio decreased from 19.0 to 9.2 (2.1 folds). The effect of Bis in increasing the compression modulus showed a limit. After the Bis content reached 1.4 mol%, the compression modulus curve started to level off. More crosslinker did not further increase the compression modulus. However, by using more Ac-Di-Sol or Crospovidone, much stronger hydrogels could be made. Increasing the concentration of Bis alone could not make the hydrogels as strong as the Ac-Di-Sol or Crospovidone reinforced hydrogel composites. Between Ac-Di-Sol and Crospovidone XL, Ac-Di-Sol was a better choice in making the hydrogel composites. In addition to the above mentioned materials, other fibers can also be used to improve the mechanical properties of hydrogel composites. We have found that when short cotton fibers (1~4 mm) were incorporated in polyacrylamide hydrogels, the compression modulus was significantly improved.

VII. GASTRIC RETENTION OF SUPERPOROUS HYDROGELS AND SUPERPOROUS HYDROGEL COMPOSITES

The importance of controlled drug delivery systems that releases active ingredients over an extended period of time has long been recognized in pharmaceutical research. It provides great convenience to the patients and improves the therapeutic efficacy by maintaining a consistent and uniform blood level of medication over an extended period of time. Of the many routes of drug delivery, oral administration remains the most convenient and commonly employed means of introducing drugs to the systemic circulation. The duration of oral controlled drug delivery is limited by the time that the oral dosage forms remain in the upper small intestine. All of the oral dosage forms without suitable platforms are emptied from the stomach in an hour or so and pass through the upper small intestine in less than a few hours. Since most drugs are absorbed only from the upper small intestine, they have to be administered a few times a day, unless the drug has a long half-life.

Gastric retention devices are designed to prolong the retention time of a dosage form in the stomach to realize the long-term oral drug delivery. We have used a hydrogel platform for oral drug delivery for up to 50 hours after a single administration (2). In those studies, however, the hydrogel dosage form had to be preswollen to prevent premature emptying of the dosage form from the stomach due to the slow swelling to a desired size. The use of superporous hydrogels and their composites solve the problems associated with slow swelling and the weak mechanical strength.

This section describes a unique application of superporous hydrogel composites as a gastric retention device.

A. Principle and Requirements for Gastric Retention of Superporous Hydrogels and Superporous Hydrogel Composites

1. Principle of the gastric retention

The gastric retention of superporous hydrogels is based on their fast swelling property. The idea of the gastric retention is described in Fig. 7. A superporous hydrogel or its composite is encapsulated in a capsule so that the initial volume is small enough for easy swallowing (Fig. 7-A). After oral administration, it swells quickly (in less than 10 min including the dissolution of the gelatin capsule) in the

gastric juice to a large size so that its emptying into the intestine is prevented (Fig. 7--B). The superporous hydrogel or its composite may contain drugs for controlled release. The superporous hydrogel or its composite can be slowly degraded in the stomach by either mechanical force, or chemical or enzymatic hydrolysis of the polymer chains constituting the hydrogel (Fig. 7-C). Eventually, the degraded superporous hydrogel or its composite is eliminated from the stomach (Fig. 7-D).

2. Requirements for gastric retention of superporous hydrogels or superporous hydrogel composites

For the practical application as a gastric retention device, the superporous hydrogels must possess the following properties. They should be small enough for easy swallowing. In our study, size 000 hard gelatin capsules were used to house the superporous hydrogels and their composites. They also have to swell fast to prevent premature emptying into the intestine. We have found that complete swelling in less than 10 min was fast enough. The size of the swollen superporous hydrogels or their composites have to be big enough to be retained in the stomach. The diameter of the pyloric sphincter is about 2 cm in human. Under normal condition, the pylorus sphincter is closed. However, it could be stretched and pass an object even larger than 2 cm. Finally, the fully swollen superporous hydrogels or their composites have to be strong enough to withstand the peristaltic contraction by the gastric tissues (B-1~B-5 in Fig. 7).

B. Gastric Retention of Superporous Hydrogels and Superporous Hydrogel Composites

1. Radiopaque marker and image analysis

For in vivo gastric retention experiment, radiopaque markers were used to locate the exact position of superporous hydrogels or their composites in the gastrointestinal tract. Small hydrogel pellets containing $BaSO_4$ were used as the X-ray marker.

The $BaSO_4$-containing hydrogel pellets were prepared in a thin plastic tube (inner diameter of 3.35 mm). The following components were sequentially mixed in a glass vial: 1300 μl of 50% AM; 800 μl of 2.5% Bis; 150 μl of 20% APS; 1300 μl of 40% $BaSO_4$ suspension (E-Z-EM, Inc.); and 80 μl of 20% TEMED. The vial was swirled to mix the ingredients after each component was added. The mixture was then injected into the plastic tube. The gelling of the mixture started within 5 min after the addition of TEMED. After curing for 1 h at room temperature, the noodle-like gel was retrieved from the plastic tube, cut into small segments, and dried in 60°C oven for 5 h. The dried gel pellets were white and had diameter of 2 mm and length of 2 mm. To incorporate the $BaSO_4$-containing hydrogel pellets into a superporous hydrogel or its composite, two to six pellets were placed in the monomer solution (Example 10 in Section III. D. Examples of Superporous Hydrogel Preparation) before adding APS. After the addition of $NaHCO_3$, the mixture was mechanical stirred for 5~10 sec to evenly distribute the pellets.

$BaSO_4$-containing hydrogel pellets gave the following advantages. They have very high contrast over background and therefore are easy to monitor even after they are swollen for several days. The size of the dried hydrogel pellets is very small so that it does not affect the packing of a superporous hydrogel into a gelatin capsule. Several pellets can be dispersed in a superporous hydrogel so that the fragmentation of the superporous hydrogel can be easily monitored.

2. In vivo study in the canine model

The superporous hydrogels that were placed inside gelatin capsules were tested in dogs for gastric retention. Superporous hydrogels with different properties were tested under fasted or fed conditions. The dogs used in all experiments were about 50 pounds. The fasted condition was achieved by holding a dog from foods for 36 h, but the dog had free access to water. The fed condition was achieved by giving a dog 447 g of canned food right before the oral administration of the capsule. In each experiment (fasted state or fed state), the dog was given 300 ml water by stomach tube right before the oral administration of the capsule. Then the capsule containing the superporous hydrogel was swallowed by the dog with no water. X-ray pictures were taken at different time intervals after the administration of the capsule. The following is an example of the gastric retention experiments done in our laboratory.

In simulated gastric fluid, the superporous hydrogel was 2.4 cm in diameter and 3.5 cm in length. The UCP was 370 cm water pressure. Three $BaSO_4$-containing hydrogel pellets were incorporated in the superporous hydrogel as radiographic markers. The dog was in the fed state in the beginning of the study. The fed state was maintained for 6 h. After that, no food was found in the stomach and the dog was in the fasted state. The dog had free access to water throughout the experiment.

X-ray pictures were taken at time 0, 30 min, 1 h, 2 h, 3 h, 4 h, 5 h, 6 h, 7 h, 8 h, 23 h, 27 h, and 32 h. X-ray images taken at times 27 h and at 32 h are shown in Fig. 8-A and Fig. 8-B, respectively. From time 0 to time 27 h, all three $BaSO_4$-containing hydrogel markers (labeled as 1, 2, and 3) were seen in the superporous hydrogel. These markers maintained their relative positions, indicating that the superporous hydrogel remained intact. The image taken at time 32 h (Fig. 8-B) shows that one of the marker (#1) was gone to the small bowel while the other two (#2 and 3) remained in the stomach. This means that the fragmentation started between times 27 h and 32 h probably due to the repetitive gastric contractions. Once the fragmentation starts, the superporous hydrogel is expected to be emptied quickly due to the reduced size.

This experiment clearly shows that the improved mechanical strength can prolong the gastric retention time to more than 27 h. The size of the superporous hydrogel in this experiment was large enough to be retained in the stomach, and also the mechanical strength was high enough to withstand the gastric contraction force.

VIII. APPLICATIONS

Superporous hydrogels and superporous hydrogel composites can be used in various areas as briefly described below.

A. Superabsorbent Area

Due to the excellent suction capacity of superporous hydrogels and superporous hydrogel composites, they are ideal in the improvement of surgical pads for bleeding control and personal hygiene products such as disposable diapers and sanitary napkins. The fast water-absorbing property also allows application of the superporous hydrogels or their composites as a desiccating agent in replace of silica gels. Currently, all the commercially available superabsorbents are in the powder form because particulate gels with only a small size can swell fast. This brings limitations in certain applications (32). The superporous hydrogel and superporous

hydrogel composites technique allows preparation of superabsorbent materials in any size and in any shape. Superporous hydrogels are also easy to make and show a number of superior properties to the existing products, especially in their swelling rate. These merits would greatly broaden the applications of superabsorbent polymers. The superporous hydrogels technique can be used to make a wide array of synthetic, semi-synthetic, or natural superporous hydrogels which may replace the existing superabsorbents in many applications.

B. Controlled Drug Delivery

In the controlled drug delivery area, superporous hydrogels and superporous hydrogel composites can be used as a platform for long-term oral drug delivery. Due to the fast swelling and superswelling properties, they can stay in the stomach for a few hours up to more than 24 hours (4). Such a long-term gastric retention time is ideal for long-term oral controlled drug delivery.

C. Diet Control

In the diet control area, superporous hydrogels and superporous hydrogel composites can be used to control the appetite of healthy people who desire to reduce the volume of food they take. Because of the fast swelling to a very large size, superporous hydrogels and superporous hydrogel composites can remain in the stomach for extended periods of time ranging from hours to days (2-4). The presence of bulky superporous hydrogels and superporous hydrogel composites will reduce the space in the stomach and thus the amount of food that can be taken. Thus, they can be used as an alternative therapy for obesity.

D. Biomedical Area

In biomedical area, they can be used in making devices for artificial pancreas; artificial cornea; artificial skin; articular cartilage; soft tissue substitutes; cell growth substrates in tissue engineering; burn dressings; surgical augmentation of the female breast; or haemoperfusion in blood detoxification and in the treatment of uraemia, among others.

E. Biotechnology

In the biotechnology area, they can be used in separation of macromolecules and cells from the medium. The presence of extremely large pores makes superporous hydrogels and superporous hydrogel composites are also ideal materials for chromatographic supports.

F. Structural Applications

The low density of superporous hydrogels and superporous hydrogel composites allows applications as a high-strength, light-weight structural material as well as a packaging material. They will be also good as insulators and fillers in structures with energy-sensitive applications.

G. Fast responsive stimuli-sensitive superporous hydrogels

Hydrogels which can change their volume rather abruptly upon small changes in environmental conditions are known as "intelligent" or "smart" hydrogels. Smart hydrogels respond to changes in the environmental conditions, such as temperature,

pH, solvent, electric field, specific molecules or ions, light, or pressure. While these smart hydrogels are highly useful in various applications, the typical response time usually ranges from hours to days, and this slow response time sometimes limits the usefulness of the smart hydrogels. By making superporous smart hydrogels, the response time could be reduced to seconds or minutes.

IX. SUMMARY OF IMPORTANT POINTS

A. New Features in the Preparation of Hydrogel Composites and Superporous Hydrogel Composites

1. Easy control of pore size

The average pore size in the superporous hydrogels is several hundred micrometers. The pore size can be controlled very easily using the technique described in this disclosure. One of the advantages of the superporous hydrogels and superporous hydrogel composites described here is that the pore size can be controlled independent of the crosslink density (41).

2. Synthesis of hydrogel composites and superporous hydrogel composites

To date, numerous hydrogels have been made by changing the composition of monomers to make hydrogels of random copolymers or block copolymers. However, hydrogels containing hydrophilic, particulate composite materials as a crosslinking agent have not been synthesized so far. Hydrogels and superporous hydrogels synthesized in the presence of hydrophilic, particulate composite materials, such as microcrystalline cellulose crystals, crosslinked sodium carboxymethylcellulose (Ac-Di-Sol®), cross-linked sodium starch glycolate (Primojel® and Explotab®), crosslinked PVP (Crospovidone®), possess unique properties which could not be obtained otherwise.

3. Stabilization of foams by composite materials during synthesis of superporous hydrogel composites

One of the important roles of Ac-Di-Sol® is to stabilize the foam during synthesis. The total amount of acid used in Example 10 was very small compared with that used other examples, and thus the total amount of gas bubbles generated were also small. Since it is desirable to have superporous hydrogels with a well-connected and uniformly-distributed intercellular capillary channel system (which is essential for fast swelling), the limited amount of gas bubbles need to be well preserved during the preparation. To examine the foam stabilizing effect of Ac-Di-Sol®, four types of superporous hydrogels were prepared based on Example 10: (A) in the absence of Pluronic® F127; (B) in the absence of Ac-Di-Sol®; (C) in the presence of both Pluronic® F127 and Ac-Di-Sol®; (d) in the absence of Ac-Di-Sol® but with two times more acrylic acid (AA) (i.e., 60 µl instead of 30 µl of 50% AA). Only sample (C) had high swelling rate and good mechanical strength, indicating the presence of the interconnected pores. The SEM pictures showed interconnected pores in Sample (C). This study has clearly shown that Ac-Di-Sol® is important in making interconnected channels in superporous hydrogels when small amount of blowing agent is used.

4. Ethanol drying of superporous hydrogels

The drying of the superporous hydrogels after replacing water with ethanol (or other organic solvents) has a few advantages. Ethanol precipitates polymer chains and thus makes the pores formed by polymer chains less prone to collapse. This results in maintaining of the open capillaries even after drying. Thus, swelling of superporous hydrogels dried with ethanol is much faster than control superporous hydrogels dried without ethanol treatment.

5. Air drying of superporous hydrogel composites

While the ethanol drying method results in superporous hydrogels that swell fast from the dried state, use of ethanol is costly compared to simple air drying. The air-dried superporous hydrogel composites maintain the ability to swell fast as the ethanol dried superporous hydrogels. The air drying of superporous hydrogel composites is an economical way of preparing dried hydrogels that swell fast.

6. Increasing wettability by partial moistening

Moistening the dried superporous hydrogels improved the wettability of the capillary channels. Thus, superporous hydrogels or superporous hydrogel composites can be moistened for improving the swelling property. If the presence of the moisture during storage may cause a problem, we can take advantage of the following phenomenon. The surface of a hydrated hydrogel is amphiphilic and can become hydrophilic when in contact of hydrophilic surface but hydrophobic when in contact with hydrophobic surface.

The superporous hydrogels and their composites can be dehydrated and/or dried. Then, they can be moistened in a moisture chamber to absorb ~100% of their original weight water. The size of the dried superporous hydrogels and their composites does not change much after this moistening. The moistened superporous hydrogels and their composites can be freeze dried for long-term storage.

After superporous hydrogels and their composites in the dry state absorb moisture in moisture chamber, the hydrophilic groups reorient to the outside so that the surface becomes hydrophilic. When the moistened superporous hydrogels are frozen, the polymer chains are expected to lose their mobility and keep the surface hydrophilic. Thus, the freeze-dried superporous hydrogels and their composites will maintain high wettability even after complete drying by freeze-drying. This approach is totally different from freeze-drying of superporous hydrogels and their composites in the fully swollen state. Freeze-drying in the fully swollen state will result in large sized, dried gels, while our approach mentioned above will have much smaller size. Another advantage of our approach is that freeze-drying of the moistened, superporous hydrogels will be much faster than that of fully swollen superporous hydrogels..

B. Unique Properties of Superporous Hydrogels and Superporous Hydrogel Composites

1. Fast Swelling

Fast swelling rate and large swelling size are the most distinctive properties of the superporous hydrogels. Two factors, i.e. the wettability and the capillary channels, are most important in affecting the swelling rate of superporous hydrogels. Any

factors that promote these two properties will improve the swelling rate of superporous hydrogels.

The air-dried superporous hydrogels do not have good capillary channels due to their collapse during the drying process. Ethanol dehydration can effectively protect the capillary channels and thus greatly improve the swelling kinetics. Voranol® as a wetting agent can improve the wettability of superporous hydrogels and therefore increase the swelling speed. Moistening of the superporous hydrogel surface can also improve the wettability and thus increase the swelling kinetics. Superdisintegrants such as Ac-Di-Sol® and Primojel® increase the swelling kinetics by protecting the capillary channels and improving wettability.

2. Superabsorbent Property

Any polymeric materials that can swell more than 20 times of its dry weight in aqueous solution is called superabsorbent polymers (SAP). High water absorbency and fast swelling kinetics are two most desirable properties of SAP. Superporous hydrogels, due to their unique structural properties, can absorb much more water and swell much faster in aqueous solution than the conventional non-porous and macroporous hydrogels. For this reason, superporous hydrogels are ideal as superabsorbent materials.

Existing superabsorbents used in baby diapers are made by complicated processes and some of which involve the use of organic solvents (35). The use of organic solvent may raise safety and environmental concerns. Currently, all the commercially available superabsorbents are in the powder form because particulate gels with only a small size can swell fast. This brings limitations in certain applications (32). The superporous hydrogel technique allows preparation of superabsorbent materials in any size and in any shape. Superporous hydrogels and their composites are also easy to make and show a number of superior properties to the existing products, especially in their swelling rate. These merits would greatly broaden the applications of superabsorbent polymers. The superporous hydrogels technique can be used to make a wide array of synthetic, semi-synthetic, or natural superporous hydrogels which may replace the existing superabsorbents in certain applications.

3. High Mechanical Strength

The main drawback of superporous hydrogels is that they do not have high mechanical strength. It has been the general observation that porous hydrogels with pore sizes above 40~50 μm are too weak to maintain the intact structure upon applying force and thus are not suitable to serve as a weight-bearing material (9,12). The presence of composite materials in the superporous hydrogels makes them mechanically very strong. The superporous hydrogels prepared in Example 10 are so strong that they can actually bounce back without breaking when dropped onto the floor.

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Table 1. Vinyl monomers used for making superporous hydrogels.

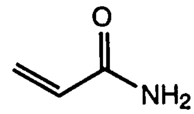
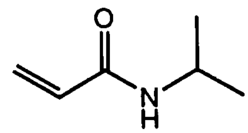
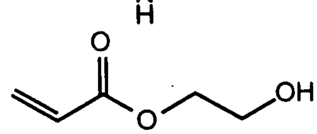
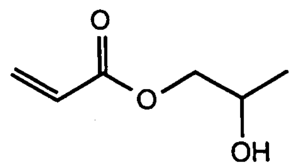
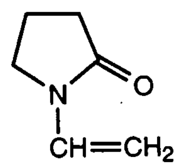
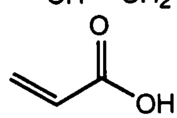
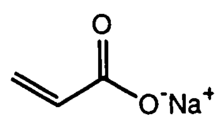
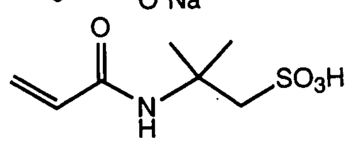
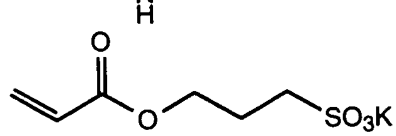
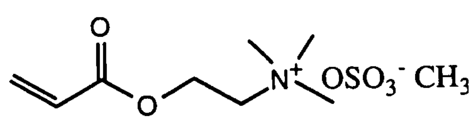
Chemical name (and abbreviation)	Monomer structure
Acrylamide (AM)	
N-isopropylacrylamide (NIPAM)	
2-hydroxyethyl methacrylate (HEMA)	
2-hydroxypropyl methacrylate (HPMA)	
N-vinyl pyrrolidinone (VP)	
Acrylic acid (AA)	
Sodium acrylate	
2-acrylamido-2-methyl-1-propanesulfonic acid (AMPS)	
3-sulfopropyl acrylate, potassium salt (SPAK)	
2-(acryloyloxy)ethyltrimethyl-ammonium methyl sulfate (ATMS)	

Table 2. The dimension, density, swelling ratio, and swelling time of poly(acrylic acid-co-acrylamide) superporous hydrogels and superporous hydrogel composites treated by different processes.

Sample #	Description	Dimension: diameter (mm) x height (mm)	Density of the dried superporous hydrogel (g/cm^3)	Swelling ratio	Swelling time
1	Non-porous hydrogel (control)	4.8 x 2.3	1.30 ± 0.08	173 ± 7	720 ± 110 min
2	Superporous hydrogel which was oven-dried after synthesis	5.8 x 2.8	0.76 ± 0.05	328 ± 40	31 ± 6 min
3	Superporous hydrogel which was fully swollen in DDW and then oven-dried	5.8 x 2.7	0.80 ± 0.06	307 ± 29	51 ± 22 min
4	Superporous hydrogel which was dehydrated by ethanol after synthesis and then oven-dried	8.0 x 4.0	0.26 ± 0.02	355 ± 54	4.8 ± 1.5 min
5	Superporous hydrogel which was swollen in DDW, dehydrated by ethanol, and then oven-dried	10.7 x 5.4	0.13 ± 0.02	337 ± 76	4.1 ± 0.3 min
6	Superporous hydrogel which was dehyedrated by ethanol (containing 1% Voranol$_{240\text{-}800}$®) after synthesis, and then oven-dried	8.1 x 4.0	0.25 ± 0.02	368 ± 34	2.8 ± 0.7 min
7	Sample #2 absorbed 126 ± 11% (of its original weight) moisture.	5.9 x 2.9	0.76 ± 0.05	339 ± 36	7 ± 6 min
8	Sample #4 absorbed 81 ± 4% (of its original weight) moisture.	8.2 x 4.1	0.26 ± 0.02	334 ± 10	37 ± 3 sec

9	Superporous hydrogel which was synthesized by adding 50 mg of Ac-Di-Sol® to the monomer solution and then oven-dried	6.7 x 3.3	0.48 ± 0.05	294 ± 44	8.5 ± 6.1 min
10	Superporous hydrogel which was synthesized by adding 100 mg of Ac-Di-Sol® to the monomer solution and then oven-dried	7.2 x 3.5	0.39 ± 0.02	192 ± 18	1.2 ± 0.6 min
11	Superporous hydrogel which was synthesized by adding 150 mg of Ac-Di-Sol® to the monomer solution and then oven-dried	7.5 x 3.8	0.33 ± 0.04	120 ± 23	35 ± 9 sec
12	Superporous hydrogel which was synthesized by adding 200 mg of Ac-Di-Sol® to the monomer solution and then oven-dried	7.9 x 4.0	0.28 ± 0.01	91 ± 22	22 ± 4 sec
13	Bis was 0.6 mol% of monomers (Sample #1~12 contained Bis of 0.3 mol% of monomers). SPH was oven-dried after synthesis.	6.8 x 3.3	0.45 ± 0.04	231 ± 12	13.4 ± 2.1min
14	Bis was 0.9 mol% of monomers. SPH was oven-dried after synthesis.	7.2 x 3.6	0.38 ± 0.03	166 ± 26	3.1 ± 2.5 min

All samples were prepared based on Example 9 in Section III. D. Examples of Superporous Hydrogel Preparation.

No PF127 and $NaHCO_3$ was used in Sample #1.
In Sample #9~12, different amounts of Ac-Di-Sol® were added.
In Sample #13 and 14, different amounts of Bis were added.

The swelling ratio was tested in deionized destilled water (DDW). The swelling time is the time to reach the equilibrium swelling after a superporous hydrogel or a superporous hydrogel composite is placed in DDW. To measure the swelling time, a superporous hydrogel or a superporous hydrogel composite in disk shape (50 mg to 65 mg in weight) was tested.

At least three samples were tested for each measurement.

Table 3. Hydrogel composites made of polyacrylamide and Ac-Di-Sol fibers or Crospovidone XL.

Polyacrylamide - Ac-Di-Sol composites

Sample	Ac-Di-Sol : AM (w:w)	% weight of Ac-Di-Sol in dried hydrogels	Swelling ratio	Compression modulus E_c (kg/cm^2)
1	0 : 100	0	19.0	0.25
2	11 : 100	10	15.3	0.28
3	25 : 100	20	13.6	0.38
4	43 : 100	30	11.1	0.53
5	67 : 100	40	9.5	0.92
6	100 : 100	50	8.0	1.17

Polyacrylamide - Crospovidone XL composites

Sample	Crospovidone XL : AM (w/w)	% weight of Crospovidone XL in dried hydrogels	Swelling ratio	Compression modulus E_c (kg/cm^2)
7	0 : 100	0	19.0	0.25
8	11 : 100	10	14.9	0.25
9	25 : 100	20	12.3	0.25
10	43 : 100	30	9.5	0.33
11	67 : 100	40	7.7	0.48
12	100 : 100	50	5.9	0.64
13	150 : 100	60	4.3	1.07